

FORM PTO-1390 (REV 10-2000)		U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTORNEY'S DOCKET NUMBER GIN-6718CP5US
TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C.371			U.S. APPLICATION NO. (If known, see 37 CFR 1.5) 097743247
INTERNATIONAL APPLICATION PCT/JP99/03929	INTERNATIONAL FILING DATE 22 July 1999 (22.07.99)	PRIORITY DATE CLAIMED 24 July 1998 (24.07.98)	
TITLE OF INVENTION HUMAN PROTEINS HAVING HYDROPHOBIC DOMAINS AND DNAs ENCODING THESE PROTEINS			
APPLICANT(S) FOR DO/EO/US Seishi KATO and Tomoko KIMURA			
Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:			
<ol style="list-style-type: none"> 1. <input checked="" type="checkbox"/> This is a FIRST submission of items concerning a filing under 35 U.S.C.371. 2. <input type="checkbox"/> This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371. 3. <input type="checkbox"/> This is an express request to promptly begin national examination procedures (35 U.S.C. 371(f)). 4. <input checked="" type="checkbox"/> The US has been elected by the expiration of 19 months from the priority date (PCT Article 31). 5. <input checked="" type="checkbox"/> A copy of the International Application as filed (35 U.S.C. 371(c)(2)) <ol style="list-style-type: none"> a. <input type="checkbox"/> is attached hereto (required only if not communicated by the International Bureau). b. <input checked="" type="checkbox"/> has been communicated by the International Bureau. c. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US). 6. <input type="checkbox"/> An English language translation of the International Application as filed (35 U.S.C 371(c)(2)). 7. <input checked="" type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)) <ol style="list-style-type: none"> a. <input type="checkbox"/> are attached hereto (required only if not communicated by the International Bureau). b. <input type="checkbox"/> have been communicated by the International Bureau. c. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired. d. <input checked="" type="checkbox"/> have not been made and will not be made. 8. <input type="checkbox"/> An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)). 9. <input type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). 10. <input type="checkbox"/> An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)). 			
Items 11. to 16. below concern document(s) or information included:			
<ol style="list-style-type: none"> 11. <input type="checkbox"/> An Information Disclosure Statement under 37 CFR 1.97 and 1.98. 12. <input type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included 13. <input type="checkbox"/> A FIRST preliminary amendment. <input type="checkbox"/> A SECOND or SUBSEQUENT preliminary amendment. 14. <input type="checkbox"/> A substitute specification. 15. <input type="checkbox"/> A change of power of attorney and/or address letter. 16. <input checked="" type="checkbox"/> Other items or information: Transmittal Letter (2 sheets in duplicate); PCT Request and Fee Calculation Sheet (6 sheets); PCT Notification of Receipt of Record Copy (Form PCT/IB/301) (3 sheets); PCT Notification of Receipt of Search Copy (1 sheet); PCT Notification Concerning Submission of Priority Document (JP 10/208820 filed 24 July 1998) (PCT/IB/304) (1 sheet); PCT International Published Application (WO 00/05367) (without International Search Report) (351 sheets); Cover of PCT International Published Application (WO 00/05367) (with International Search Report attached) (12 sheets); PCT Notification of Transmittal of the International Search Report or the Declaration (14 sheets); PCT Notice Informing the Applicant of the Communication of the International Application to the Designated Offices (PCT/IB/308) (1 sheet); PCT Information Concerning Elected Offices Notified of their Election (PCT/IB/332) (1 sheet); PCT Notification of Receipt of Demand by Competent International Preliminary Examining Authority (1 sheet); PCT Written Opinion (NO RESPONSE NECESSARY) (4 sheets); Notification of Transmittal of the International Preliminary Examination Report (6 sheets); Check (#040892) (\$1130) based on large entity; Certificate of Express Mailing (1 sheet); and Return Postcard. 			

U.S. APPLICATION NO. (if known, see 37 CFR 1.5) 09/743247		INTERNATIONAL APPLICATION NO. PCT/JP99/03929		ATTORNEY'S DOCKET NO. GIN-6718CP5US	
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17. <input checked="" type="checkbox"/> The following fees are submitted: BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)) (a/o November 1, 2000): Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO.....\$1000 International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO\$860 International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.455(a)(2)) paid to USPTO\$710 International preliminary examination fee paid to USPTO (37 CFR 1.482) but all claims did not satisfy provisions of PCT Article 33(1)-(4).....\$690 International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4).....\$100 <div style="text-align: center;">ENTER APPROPRIATE BASIC FEE AMOUNT =</div>				CALCULATIONS PTO USE ONLY <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 50%; text-align: center;">\$860</td> <td style="width: 50%;"></td> </tr> </table>		\$860	
\$860							

Surcharge of \$130.00 for furnishing the oath or declaration later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(e)).				\$--	
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CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE		
Total claims	10 -20 =	0	X \$18.00	\$0	
Independent claims	2 -3 =	0	X \$80.00	\$0	
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ 270.00	\$270	
TOTAL OF ABOVE CALCULATIONS =				\$1130	

<input type="checkbox"/> Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by 1/2.				\$--	
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SUBTOTAL =				\$1130	
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Processing fee of \$130.00 for furnishing the English translation later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(f)).				\$--	
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TOTAL NATIONAL FEE =				\$1130	
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Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property +				\$--	
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TOTAL FEES ENCLOSED =				\$1130	
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				Amount to be:	
				refunded	
				charged	

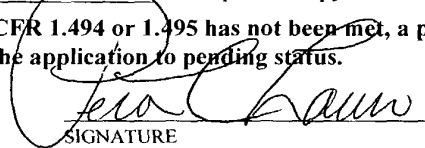
a. ☒ A check (#040892) in the amount of \$1130 to cover the above fees is enclosed.

b. ☐ Please charge my Deposit Account No. _____ in the amount of \$ _____ to cover the above fees.
 A duplicate copy of this sheet is enclosed.

c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit
 any overpayment to Deposit Account No. 12-0080. A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

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534 Rec'd PCT/PTO 05 JAN 2001

DESCRIPTION

Human Proteins Having Hydrophobic
Domains and DNAs Encoding These Proteins

5

TECHNICAL FIELD

The present invention relates to human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as eucaryotic cells expressing these DNAs. The proteins of the present invention can be employed as pharmaceuticals or as antigens for preparing antibodies against these proteins. The human cDNAs of the present invention can be utilized as probes for the genetic diagnosis and gene sources for the gene therapy. Furthermore, the cDNAs can be utilized as gene sources for large-scale production of the proteins encoded by these cDNAs. Cells into which these genes are introduced to express secretory proteins and membrane proteins in large amounts can be utilized for detection of the corresponding receptors and ligands, screening of novel low-molecular pharmaceuticals, and so on.

BACKGROUND ART

Cells secrete many proteins outside the cells. These secretory proteins play important roles for the proliferation control, the differentiation induction, the material transportation, the biological protection, etc. in the cells. Different from intracellular proteins, the secretory proteins exert their actions outside the cells, whereby they can be administered in the intracorporeal manner such as the injection or the drip, so that there are

hidden potentialities as medicines. In fact, a number of human secretory proteins such as interferons, interleukins, erythropoietin, thrombolytic agents, etc. have been currently employed as medicines. In addition, secretory proteins other than those described above have been undergoing clinical trials to develop as pharmaceuticals. Because it has been conceived that the human cells still produce many unknown secretory proteins, availability of these secretory proteins as well as genes coding for them is expected to lead to development of novel pharmaceuticals utilizing these proteins.

On the other hand, membrane proteins play important roles, as signal receptors, ion channels, transporters, etc. in the material transportation and the information transmission through the cell membrane. Examples thereof include receptors for a variety of cytokines, ion channels for the sodium ion, the potassium ion, the chloride ion, etc., transporters for saccharides and amino acids, and so on, where the genes for many of them have been cloned already. It has been clarified that abnormalities of these membrane proteins are associated with a number of hitherto-cryptogenic diseases. Therefore, discovery of a new membrane protein is anticipated to lead to elucidation of the causes of many diseases, so that isolation of a new gene coding for the membrane protein has been desired.

Heretofore, owing to difficulty in the purification from human cells, these secretory proteins and membrane proteins have been isolated by an approach from the gene side. A general method is the so-called expression cloning which comprises introduction of a cDNA library into eucaryotic cells to express cDNAs and then screening of the cells secreting, or expressing on the surface of membrane,

the objective active protein. However, this method is applicable only to cloning of a gene for a protein with a known function.

In general, secretory proteins and membrane proteins possess at least one hydrophobic domain inside the proteins, wherein, after synthesis thereof in the ribosome, this domain works as a secretory signal or remains in the phospholipid membrane to be trapped in the membrane. Accordingly, the evidence of this cDNA for encoding a secretory protein and a membrane protein is provided by determination of the whole base sequence of a full-length cDNA followed by detection of highly hydrophobic domain(s) in the amino acid sequence of the protein encoded by this cDNA.

OBJECTS OF THE INVENTION

The main object of the present invention is to provide novel human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as transformed eucaryotic cells that are capable of expressing these DNAs. This object as well as other objects and advantages of the present invention will become apparent to those skilled in the art from the following description with reference to the accompanying drawings.

BRIEF DESCRIPTION OF DRAWINGS

Fig. 1 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01550.

Fig. 2 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02593.

Fig. 3 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10195.

Fig. 4 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10423.

Fig. 5 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10506.

5 Fig. 6 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10507.

Fig. 7 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10548.

10 Fig. 8 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10566.

Fig. 9 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10567.

Fig. 10 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10568.

15 Fig. 11 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01426.

Fig. 12 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02515.

20 Fig. 13 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02575.

Fig. 14 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10357.

Fig. 15 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10447.

25 Fig. 16 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10477.

Fig. 17 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10513.

30 Fig. 18 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10540.

Fig. 19 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10557.

Fig. 20 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10563.

Fig. 21 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01467.

5 Fig. 22 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01956.

Fig. 23 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02545.

10 Fig. 24 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02551.

Fig. 25 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02631.

Fig. 26 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02632.

15 Fig. 27 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10488.

Fig. 28 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10538.

20 Fig. 29 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10542.

Fig. 30 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10571.

Fig. 31 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01470.

25 Fig. 32 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02419.

Fig. 33 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02631.

30 Fig. 34 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02695.

Fig. 35 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10031.

Fig. 36 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10530.

Fig. 37 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10541.

5 Fig. 38 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10550.

Fig. 39 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10590.

10 Fig. 40 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10591.

Fig. 41 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01462.

Fig. 42 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02485.

15 Fig. 43 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02798.

Fig. 44 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10041.

20 Fig. 45 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10246.

Fig. 46 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10392.

Fig. 47 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10489.

25 Fig. 48 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10519.

Fig. 49 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10531.

30 Fig. 50 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10574.

SUMMARY OF THE INVENTION

As the result of intensive studies, the present inventors have been successful in cloning of cDNAs coding for proteins having hydrophobic domains from the human full-length cDNA bank, thereby completing the present invention.

5 In other words, the present invention provides human proteins having hydrophobic domains, namely proteins comprising any of the amino acid sequences represented by SEQ ID Nos. 1 to 10, 31 to 40, 61 to 70, 91 to 100, and 121 to 130. Moreover, the present invention provides DNAs coding
10 for the above-mentioned proteins, exemplified by cDNAs comprising any of the base sequences represented by SEQ ID Nos. 11 to 20, 41 to 50, 71 to 80, 101 to 110, and 131 to 140, as well as expression vectors that are capable of expressing any of these DNAs by in vitro translation or in
15 eucaryotic cells and transformed eucaryotic cells that are capable of expressing these DNAs and of producing the above-mentioned proteins.

DETAILED DESCRIPTION OF THE INVENTION

20 The proteins of the present invention can be obtained, for example, by a method for isolation from human organs, cell lines, etc., a method for preparation of peptides by the chemical synthesis, or a method for production with the recombinant DNA technology using the DNAs coding for the
25 hydrophobic domains of the present invention, among which the method for production with the recombinant DNA technology is employed preferably. For instance, in vitro expression of the proteins can be achieved by preparation of an RNA by in vitro transcription from a vector having one of
30 the cDNAs of the present invention, followed by in vitro translation using this RNA as a template. Also, introduction of the translated region into a suitable expression vector

by the method known in the art leads to expression of a large amount of the encoded protein in prokaryotic cells such as *Escherichia coli*, *Bacillus subtilis*, etc., and eucaryotic cells such as yeasts, insect cells, mammalian cells, etc.

In the case where one of the proteins of the present invention is produced by expressing the DNA by in vitro translation, the protein of the present invention can be produced in vitro, when the translated region of this cDNA is introduced into a vector having an RNA polymerase promoter, followed by addition of the vector to an in vitro translation system such as a rabbit reticulocyte lysate or a wheat germ extract, containing an RNA polymerase corresponding to the promoter. RNA polymerase promoters are exemplified by T7, T3, SP6, and the like. The vectors containing these RNA polymerase promoters are exemplified by pKA1, pCDM8, pT3/T7 18, pT7/3 19, pBluescript II, and so on. Furthermore, the protein of the present invention can be expressed as the secreted form or the form incorporated into the microsome membrane, when a canine pancreas microsome or the like is added to the reaction system.

In the case where one of the protein of the present invention is produced by expressing the DNA in a microorganism such as *Escherichia coli* etc., a recombinant expression vector bearing the translated region of the cDNA of the present invention is constructed in an expression vector having an origin which can be replicated in the microorganism, a promoter, a ribosome-binding site, a cDNA-cloning site, a terminator etc. and, after transformation of the host cells with this expression vector, the resulting transformant is incubated, whereby the protein encoded by said cDNA can be produced on a large scale in the

microorganism. In this case, a protein fragment containing any region can be obtained by carrying out the expression with inserting an initiation codon and a termination codon in front of and behind the selected translated region.

5 Alternatively, a fusion protein with another protein can be expressed. Only the portion of the protein encoded by this cDNA can be obtained by cleavage of this fusion protein with a suitable protease. The expression vector for *Escherichia coli* is exemplified by the pUC series, pBluescript II, the
10 pET expression system, the pGEX expression system, and so on.

In the case where one of the proteins of the present invention is produced by expressing the DNA in eucaryotic cells, the protein of the present invention can be produced as a secretory protein or as a membrane protein on the cell-
15 membrane surface, when the translated region of this cDNA is introduced into an expression vector for eucaryotic cells that has a promoter, a splicing region, a poly(A) addition site, etc., followed by introduction into the eucaryotic cells. The expression vector is exemplified by pKA1,
20 pED6dpc2, pCDM8, pSVK3, pMSG, pSVL, pBK-CMV, pBK-RSV, EBV vector, pRS, pYES2, and so on. Examples of eucaryotic cells to be used in general include mammalian cultured cells such as simian kidney cells COS7, Chinese hamster ovary cells CHO, etc., budding yeasts, fission yeasts, silkworm cells,
25 *Xenopus* oocytes, and so on, but any eucaryotic cells may be used, provided that they are capable of expressing the proteins of the present invention. The expression vector can be introduced into the eucaryotic cells by methods known in the art such as the electroporation method, the calcium
30 phosphate method, the liposome method, the DEAE-dextran method, and so on.

After one of the proteins of the present invention is

expressed in prokaryotic cells or eucaryotic cells, the objective protein can be isolated from the culture and purified by a combination of separation procedures known in the art. Such examples include treatment with a denaturing agent such as urea or a detergent, sonication, enzymatic digestion, salting-out or solvent precipitation, dialysis, centrifugation, ultrafiltration, gel filtration, SDS-PAGE, isoelectric focusing, ion-exchange chromatography, hydrophobic chromatography, affinity chromatography, reverse phase chromatography, and so on.

The proteins of the present invention include peptide fragments (5 amino acid residues or more) containing any partial amino acid sequence in the amino acid sequences represented by SEQ ID Nos. 1. to 10, 31 to 40, 61 to 70, 91 to 100, and 121 to 130. These peptide fragments can be utilized as antigens for preparation of antibodies. Hereupon, among the proteins of the present invention, those having the signal sequences are secreted in the form of mature proteins, after the signal sequences are removed. Therefore, these mature proteins shall come within the scope of the present invention. The N-terminal amino acid sequences of the mature proteins can be easily determined by using the method for the determination of cleavage site of a signal sequence [JP 8-187100 A]. Furthermore, some membrane proteins undergo the processing on the cell surface to be converted to the secretory forms. Such proteins or peptides in the secretory forms shall come within the scope of the present invention. In the case where sugar chain-binding sites are present in the amino acid sequences, expression in appropriate eucaryotic cells affords proteins to which sugar chains are attached. Accordingly, such proteins or peptides to which sugar chains are attached shall come within the

scope of the present invention.

The DNAs of the present invention include all the DNAs coding for the above-mentioned proteins. These DNAs can be obtained by using a method by chemical synthesis, a method
5 by cDNA cloning, and so on.

The cDNAs of the present invention can be cloned, for example, from cDNA libraries derived from the human cells. These cDNAs are synthesized by using as templates poly(A)⁺ RNAs extracted from human cells. The human cells may be
10 cells delivered from the human body, for example, by the operation or may be the cultured cells. The cDNAs can be synthesized by using any method selected from the Okayama-Berg method [Okayama, H. and Berg, P., Mol. Cell. Biol. 2: 161-170 (1982)], the Gubler-Hoffman method [Gubler, U. and
15 Hoffman, J. Gene 25: 263-269 (1983)], and so on, but it is preferred to use the capping method [Kato, S. et al., Gene 150: 243-250 (1994)], as exemplified in Examples, in order to obtain a full-length clone in an effective manner. In addition, commercially available, human cDNA libraries can
20 be utilized. Cloning of the cDNAs of the present invention from the cDNA libraries can be carried out by synthesis of an oligonucleotide on the basis of base sequences of any portion in the cDNA of the present invention, followed by screening using this oligonucleotide as the probe according
25 to the colony or plaque hybridization by a method known in the art. In addition, the cDNA fragments of the present invention can be prepared by synthesis of oligonucleotides which hybridize with both termini of the objective cDNA fragment, followed by the usage of these oligonucleotides as
30 the primers for the RT-PCR method using an mRNA isolated from human cells.

The cDNAs of the present invention are characterized by

5 comprising either of the base sequences represented by SEQ ID Nos. 11 to 20, 41 to 50, 71 to 80, 101 to 110, and 131 to 140 or the base sequences represented by SEQ ID Nos. 21 to 30, 51 to 60, 81 to 90, 111 to 120, and 141 to 150. Table 1 summarizes the clone number (HP number), the cells from which the cDNA was obtained, the total base number of the cDNA, and the number of the amino acid residues of the encoded protein, for each of the cDNAs.

Table 1

SEQ ID No.	HP number	Cells	Base number	Number of amino acid residues
1, 11, 21	HP01550	Stomach cancer	510	125
2, 12, 22	HP02593	Saos-2	697	131
3, 13, 23	HP10195	HT-1080	1619	242
4, 14, 24	HP10423	U-2 OS	1066	264
5, 15, 25	HP10506	Stomach cancer	618	112
6, 16, 26	HP10507	Stomach cancer	1021	146
7, 17, 27	HP10548	Stomach cancer	1432	344
8, 18, 28	HP10566	Stomach cancer	601	97
9, 19, 29	HP10567	Stomach cancer	585	124
10, 20, 30	HP10568	Stomach cancer	1100	327
31, 41, 51	HP01426	Stomach cancer	1065	313
32, 42, 52	HP02515	Saos-2	937	229
33, 43, 53	HP02575	Saos-2	1678	467
34, 44, 54	HP10357	Stomach cancer	467	99
35, 45, 55	HP10447	Liver	875	189
36, 46, 56	HP10477	Liver	1256	363
37, 47, 57	HP10513	Stomach cancer	884	249
38, 48, 58	HP10540	Saos-2	589	98
39, 49, 59	HP10557	Stomach cancer	673	172
40, 50, 60	HP10563	Saos-2	1425	120
61, 71, 81	HP01467	HT-1080	1436	307
62, 72, 82	HP01956	Liver	997	183
63, 73, 83	HP02545	Saos-2	1753	327
64, 74, 84	HP02551	Saos-2	1117	223
65, 75, 85	HP02631	Saos-2	1380	48
66, 76, 86	HP02632	HT-1080	1503	371
67, 77, 87	HP10488	Liver	733	90
68, 78, 88	HP10538	Saos-2	3768	499
69, 79, 89	HP10542	Stomach cancer	770	106
70, 80, 90	HP10571	Stomach cancer	1229	152

91, 101, 111	HP01470	Stomach cancer	1619	358
92, 102, 112	HP02419	Stomach cancer	2054	226
93, 103, 113	HP02631	Saos-2	1380	195
94, 104, 114	HP02695	Stomach cancer	1292	339
95, 105, 115	HP10031	Saos-2	2168	487
96, 106, 116	HP10530	Saos-2	1357	393
97, 107, 117	HP10541	Stomach cancer	711	196
98, 108, 118	HP10550	Stomach cancer	651	107
99, 109, 119	HP10590	HT-1080	1310	350
100, 110, 120	HP10591	HT-1080	1400	107
121, 131, 141	HP01462	HT-1080	2050	483
122, 132, 142	HP02485	Stomach cancer	2746	334
123, 133, 143	HP02798	HT-1080	1136	267
124, 134, 144	HP10041	Saos-2	619	106
125, 135, 145	HP10246	KB	864	224
126, 136, 146	HP10392	U-2 OS	1527	258
127, 137, 147	HP10489	Stomach cancer	659	110
128, 138, 148	HP10519	Stomach cancer	710	91
129, 139, 149	HP10531	Saos-2	2182	344
130, 140, 150	HP10574	Stomach cancer	2773	428

Hereupon, the same clones as the cDNAs of the present invention can be easily obtained by screening of the cDNA libraries constructed from the human cell lines or human tissues utilized in the present invention by the use of an oligonucleotide probe synthesized on the basis of the cDNA base sequence described in any of SEQ ID Nos. 11 to 30, 41 to 60, 71 to 90, 101 to 120, and 131 to 150.

In general, the polymorphism due to the individual difference is frequently observed in human genes. Accordingly, any cDNA in which one or plural nucleotides are inserted, deleted and/or substituted with other nucleotides in SEQ ID Nos. 11 to 30, 41 to 60, 71 to 90, 101 to 120, and

131 to 150 shall come within the scope of the present invention.

In a similar manner, any protein in which one or plural amino acids are inserted, deleted and/or substituted with other amino acids shall come within the scope of the present invention, as far as the protein possesses the activity of any protein having the amino acid sequences represented by SEQ ID Nos. 1 to 10, 31 to 40, 61 to 70, 91 to 100, and 121 to 130.

The cDNAs of the present invention include cDNA fragments (10 bp or more) containing any partial base sequence in the base sequences represented by SEQ ID Nos. 11 to 20, 41 to 50, 71 to 80, 101 to 110, and 131 to 140 or in the base sequences represented by SEQ ID Nos. 21 to 30, 51 to 60, 81 to 90, 111 to 120, and 141 to 150. Also, DNA fragments consisting of a sense strand and an anti-sense strand shall come within this scope. These DNA fragments can be utilized as the probes for the genetic diagnosis.

In addition to the activities and uses described above, the polynucleotides and proteins of the present invention may exhibit one or more of the uses or biological activities (including those associated with assays cited herein) identified below. Uses or activities described for proteins of the present invention may be provided by administration or use of such proteins or by administration or use of polynucleotides encoding such proteins (such as, for example, in gene therapies or vectors suitable for introduction of DNA).

Research Uses and Utilities

The polynucleotides provided by the present invention can be used by the research community for various purposes. The polynucleotides can be used to express recombinant

protein for analysis, characterization or therapeutic use; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in disease states); as molecular weight markers on Southern gels; as chromosome markers or tags (when labeled) to identify chromosomes or to map related gene positions; to compare with endogenous DNA sequences in patients to identify potential genetic disorders; as probes to hybridize and thus discover novel, related DNA sequences; as a source of information to derive PCR primers for genetic fingerprinting; as a probe to "subtract-out" known sequences in the process of discovering other novel polynucleotides; for selecting and making oligomers for attachment to a "gene chip" or other support, including for examination of expression patterns; to raise anti-protein antibodies using DNA immunization techniques; and as an antigen to raise anti-DNA antibodies or elicit another immune response. Where the polynucleotide encodes a protein which binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the polynucleotide can also be used in interaction trap assays (such as, for example, that described in Gyuris et al., Cell 75:791-803 (1993)) to identify polynucleotides encoding the other protein with which binding occurs or to identify inhibitors of the binding interaction.

The proteins provided by the present invention can similarly be used in assay to determine biological activity, including in a panel of multiple proteins for high-throughput screening; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in assays designed to quantitatively determine

levels of the protein (or its receptor) in biological fluids; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state); and, of course, to isolate correlative receptors or ligands. Where the protein binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the protein can be used to identify the other protein with which binding occurs or to identify inhibitors of the binding interaction. Proteins involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.

Any or all of these research utilities are capable of being developed into reagent grade or kit format for commercialization as research products.

Methods for performing the uses listed above are well known to those skilled in the art. References disclosing such methods include without limitation "Molecular Cloning: A Laboratory Manual", 2d ed., Cold Spring Harbor Laboratory Press, Sambrook, J., E.F. Fritsch and T. Maniatis eds., 1989, and "Methods in Enzymology: Guide to Molecular Cloning Techniques", Academic Press, Berger, S.L. and A.R. Kimmel eds., 1987.

Nutritional Uses

Polynucleotides and proteins of the present invention can also be used as nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid supplement, use as a carbon source, use as a nitrogen source and use as a source of carbohydrate. In such cases the protein or polynucleotide of the invention can be added to the feed of a particular organism or can be

Assays for T-cell or thymocyte proliferation include without limitation those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Bertagnolli et al., J. Immunol. 145:1706-1712, 1990; Bertagnolli et al., Cellular

Immunology 133:327-341, 1991; Bertagnolli, et al., J. Immunol. 149:3778-3783, 1992; Bowman et al., J. Immunol. 152: 1756-1761, 1994.

5 Assays for cytokine production and/or proliferation of spleen cells, lymph node cells or thymocytes include, without limitation, those described in: Polyclonal T cell stimulation, Kruisbeek, A.M. and Shevach, E.M. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 3.12.1-3.12.14, John Wiley and Sons, Toronto. 1994; and
10 Measurement of mouse and human Interferon γ , Schreiber, R.D. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.8.1-6.8.8, John Wiley and Sons, Toronto. 1994.

Assays for proliferation and differentiation of hematopoietic and lymphopoietic cells include, without
15 limitation, those described in: Measurement of Human and Murine Interleukin 2 and Interleukin 4, Bottomly, K., Davis, L.S. and Lipsky, P.E. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.3.1-6.3.12, John Wiley and Sons, Toronto. 1991; deVries et al., J. Exp. Med. 173:1205-
20 1211, 1991; Moreau et al., Nature 336:690-692, 1988; Greenberger et al., Proc. Natl. Acad. Sci. U.S.A. 80:2931-2938, 1983; Measurement of mouse and human interleukin 6 - Nordan, R. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.6.1-6.6.5, John Wiley and Sons,
25 Toronto. 1991; Smith et al., Proc. Natl. Acad. Sci. U.S.A. 83:1857-1861, 1986; Measurement of human Interleukin 11 - Bennett, F., Giannotti, J., Clark, S.C. and Turner, K. J. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.15.1 John Wiley and Sons, Toronto. 1991;
30 Measurement of mouse and human Interleukin 9 - Ciarletta, A., Giannotti, J., Clark, S.C. and Turner, K.J. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp.

6.13.1, John Wiley and Sons, Toronto. 1991.

Assays for T-cell clone responses to antigens (which will identify, among others, proteins that affect APC-T cell interactions as well as direct T-cell effects by measuring proliferation and cytokine production) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function; Chapter 6, Cytokines and their cellular receptors; Chapter 7, Immunologic studies in Humans); Weinberger et al., Proc. Natl. Acad. Sci. USA 77:6091-6095, 1980; Weinberger et al., Eur. J. Immun. 11:405-411, 1981; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988.

Immune Stimulating or Suppressing Activity

A protein of the present invention may also exhibit immune stimulating or immune suppressing activity, including without limitation the activities for which assays are described herein. A protein may be useful in the treatment of various immune deficiencies and disorders (including severe combined immunodeficiency (SCID)), e.g., in regulating (up or down) growth and proliferation of T and/or B lymphocytes, as well as effecting the cytolytic activity of NK cells and other cell populations. These immune deficiencies may be genetic or be caused by viral (e.g., HIV) as well as bacterial or fungal infections, or may result from autoimmune disorders. More specifically, infectious diseases caused by viral, bacterial, fungal or other infection may be treatable using a protein of the present invention, including infections by HIV, hepatitis viruses, herpesviruses, mycobacteria, Leishmania spp., malaria spp.

and various fungal infections such as candidiasis. Of course, in this regard, a protein of the present invention may also be useful where a boost to the immune system generally may be desirable, i.e., in the treatment of cancer.

5 Autoimmune disorders which may be treated using a protein of the present invention include, for example, connective tissue disease, multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune
10 thyroiditis, insulin dependent diabetes mellitis, myasthenia gravis, graft-versus-host disease and autoimmune inflammatory eye disease. Such a protein of the present invention may also to be useful in the treatment of allergic reactions and conditions, such as asthma (particularly
15 allergic asthma) or other respiratory problems. Other conditions, in which immune suppression is desired (including, for example, organ transplantation), may also be treatable using a protein of the present invention.

Using the proteins of the invention it may also be
20 possible to immune responses, in a number of ways. Down regulation may be in the form of inhibiting or blocking an immune response already in progress or may involve preventing the induction of an immune response. The functions of activated T cells may be inhibited by
25 suppressing T cell responses or by inducing specific tolerance in T cells, or both. Immunosuppression of T cell responses is generally an active, non-antigen-specific, process which requires continuous exposure of the T cells to the suppressive agent. Tolerance, which involves inducing
30 non-responsiveness or anergy in T cells, is distinguishable from immunosuppression in that it is generally antigen-specific and persists after exposure to the tolerizing agent

has ceased. Operationally, tolerance can be demonstrated by the lack of a T cell response upon reexposure to specific antigen in the absence of the tolerizing agent.

Down regulating or preventing one or more antigen
5 functions (including without limitation B lymphocyte antigen functions (such as , for example, B7)), e.g., preventing high level lymphokine synthesis by activated T cells, will be useful in situations of tissue, skin and organ transplantation and in graft-versus-host disease (GVHD).
10 For example, blockage of T cell function should result in reduced tissue destruction in tissue transplantation. Typically, in tissue transplants, rejection of the transplant is initiated through its recognition as foreign by T cells, followed by an immune reaction that destroys the transplant. The administration of a molecule which inhibits
15 or blocks interaction of a B7 lymphocyte antigen with its natural ligand(s) on immune cells (such as a soluble, monomeric form of a peptide having B7-2 activity alone or in conjunction with a monomeric form of a peptide having an activity of another B lymphocyte antigen (e.g., B7-1, B7-3)
20 or blocking antibody), prior to transplantation can lead to the binding of the molecule to the natural ligand(s) on the immune cells without transmitting the corresponding costimulatory signal. Blocking B lymphocyte antigen
25 function in this matter prevents cytokine synthesis by immune cells, such as T cells, and thus acts as an immunosuppressant. Moreover, the lack of costimulation may also be sufficient to anergize the T cells, thereby inducing tolerance in a subject. Induction of long-term tolerance by
30 B lymphocyte antigen-blocking reagents may avoid the necessity of repeated administration of these blocking reagents. To achieve sufficient immunosuppression or

tolerance in a subject, it may also be necessary to block the function of a combination of B lymphocyte antigens.

The efficacy of particular blocking reagents in preventing organ transplant rejection or GVHD can be assessed using animal models that are predictive of efficacy in humans. Examples of appropriate systems which can be used include allogeneic cardiac grafts in rats and xenogeneic pancreatic islet cell grafts in mice, both of which have been used to examine the immunosuppressive effects of CTLA4Ig fusion proteins in vivo as described in Lenschow et al., Science 257:789-792 (1992) and Turka et al., Proc. Natl. Acad. Sci USA, 89:11102-11105 (1992). In addition, murine models of GVHD (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 846-847) can be used to determine the effect of blocking B lymphocyte antigen function in vivo on the development of that disease.

Blocking antigen function may also be therapeutically useful for treating autoimmune diseases. Many autoimmune disorders are the result of inappropriate activation of T cells that are reactive against self tissue and which promote the production of cytokines and autoantibodies involved in the pathology of the diseases. Preventing the activation of autoreactive T cells may reduce or eliminate disease symptoms. Administration of reagents which block costimulation of T cells by disrupting receptor:ligand interactions of B lymphocyte antigens can be used to inhibit T cell activation and prevent production of autoantibodies or T cell-derived cytokines which may be involved in the disease process. Additionally, blocking reagents may induce antigen-specific tolerance of autoreactive T cells which could lead to long-term relief from the disease. The efficacy of blocking reagents in preventing or alleviating

autoimmune disorders can be determined using a number of well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune encephalitis, systemic lupus erythmatosis in MRL/lpr/lpr mice or NZB hybrid mice, murine autoimmune collagen arthritis, diabetes mellitus in NOD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 840-856).

Upregulation of an antigen function (preferably a B lymphocyte antigen function), as a means of up regulating immune responses, may also be useful in therapy. Upregulation of immune responses may be in the form of enhancing an existing immune response or eliciting an initial immune response. For example, enhancing an immune response through stimulating B lymphocyte antigen function may be useful in cases of viral infection. In addition, systemic viral diseases such as influenza, the commoncold, and encephalitis might be alleviated by the administration of stimulatory forms of B lymphocyte antigens systemically.

Alternatively, anti-viral immune responses may be enhanced in an infected patient by removing T cells from the patient, costimulating the T cells in vitro with viral antigen-pulsed APCs either expressing a peptide of the present invention or together with a stimulatory form of a soluble peptide of the present invention and reintroducing the in vitro activated T cells into the patient. Another method of enhancing anti-viral immune responses would be to isolate infected cells from a patient, transfect them with a nucleic acid encoding a protein of the present invention as described herein such that the cells express all or a portion of the protein on their surface, and reintroduce the

transfected cells into the patient. The infected cells would now be capable of delivering a costimulatory signal to, and thereby activate, T cells in vivo.

5 In another application, up regulation or enhancement of antigen function (preferably B lymphocyte antigen function) may be useful in the induction of tumor immunity. Tumor cells (e.g., sarcoma, melanoma, lymphoma, leukemia, neuroblastoma, carcinoma) transfected with a nucleic acid encoding at least one peptide of the present invention can
10 be administered to a subject to overcome tumor-specific tolerance in the subject. If desired, the tumor cell can be transfected to express a combination of peptides. For example, tumor cells obtained from a patient can be transfected ex vivo with an expression vector directing the
15 expression of a peptide having B7-2-like activity alone, or in conjunction with a peptide having B7-1-like activity and/or B7-3-like activity. The transfected tumor cells are returned to the patient to result in expression of the peptides on the surface of the transfected cell.
20 Alternatively, gene therapy techniques can be used to target a tumor cell for transfection in vivo.

The presence of the peptide of the present invention having the activity of a B lymphocyte antigen(s) on the surface of the tumor cell provides the necessary
25 costimulation signal to T cells to induce a T cell mediated immune response against the transfected tumor cells. In addition, tumor cells which lack MHC class I or MHC class II molecules, or which fail to reexpress sufficient amounts of MHC class I or MHC class II molecules, can be transfected
30 with nucleic acid encoding all or a portion of (e.g., a cytoplasmic-domain truncated portion) of an MHC class I α chain protein and , microglobulin protein or an MHC class

II chain protein and an MHC class II chain protein to thereby express MHC class I or MHC class II proteins on the cell surface. Expression of the appropriate class I or class II MHC in conjunction with a peptide having the activity of a B lymphocyte antigen (e.g., B7-1, B7-2, B7-3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which blocks expression of an MHC class II associated protein, such as the invariant chain, can also be cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for thymocyte or splenocyte cytotoxicity include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Bowman et al., J.

Virology 61:1992-1998; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Brown et al., J. Immunol. 153:3079-3092, 1994.

5 Assays for T-cell-dependent immunoglobulin responses and isotype switching (which will identify, among others, proteins that modulate T-cell dependent antibody responses and that affect Th1/Th2 profiles) include, without limitation, those described in: Maliszewski, J. Immunol. 144:3028-3033, 1990; and Assays for B cell function: In
10 vitro antibody production, Mond, J.J. and Brunswick, M. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 3.8.1-3.8.16, John Wiley and Sons, Toronto. 1994.

Mixed lymphocyte reaction (MLR) assays (which will identify, among others, proteins that generate predominantly
15 Th1 and CTL responses) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse
20 Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., J. Immunol. 149:3778-3783, 1992.

Dendritic cell-dependent assays (which will identify,
25 among others, proteins expressed by dendritic cells that activate naive T-cells) include, without limitation, those described in: Guery et al., J. Immunol. 134:536-544, 1995; Inaba et al., Journal of Experimental Medicine 173:549-559, 1991; Macatonia et al., Journal of Immunology 154:5071-5079, 1995; Porgador et al., Journal of Experimental Medicine
30 182:255-260, 1995; Nair et al., Journal of Virology 67:4062-4069, 1993; Huang et al., Science 264:961-965,

1994; Macatonia et al., Journal of Experimental Medicine 169:1255-1264, 1989; Bhardwaj et al., Journal of Clinical Investigation 94:797-807, 1994; and Inaba et al., Journal of Experimental Medicine 172:631-640, 1990.

5 Assays for lymphocyte survival/apoptosis (which will identify, among others, proteins that prevent apoptosis after superantigen induction and proteins that regulate lymphocyte homeostasis) include, without limitation, those described in: Darzynkiewicz et al., Cytometry 13:795-808,
10 1992; Gorczyca et al., Leukemia 7:659-670, 1993; Gorczyca et al., Cancer Research 53:1945-1951, 1993; Itoh et al., Cell 66:233-243, 1991; Zacharchuk, Journal of Immunology 145:4037-4045, 1990; Zamai et al., Cytometry 14:891-897, 1993; Gorczyca et al., International Journal of Oncology
15 1:639-648, 1992.

 Assays for proteins that influence early steps of T-cell commitment and development include, without limitation, those described in: Antica et al., Blood 84:111-117, 1994; Fine et al., Cellular Immunology 155:111-122, 1994; Galy et
20 al., Blood 85:2770-2778, 1995; Toki et al., Proc. Nat. Acad Sci. USA 88:7548-7551, 1991.

Hematopoiesis Regulating Activity

 A protein of the present invention may be useful in regulation of hematopoiesis and, consequently, in the
25 treatment of myeloid or lymphoid cell deficiencies. Even marginal biological activity in support of colony forming cells or of factor-dependent cell lines indicates involvement in regulating hematopoiesis, e.g. in supporting the growth and proliferation of erythroid progenitor cells
30 alone or in combination with other cytokines, thereby indicating utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to

stimulate the production of erythroid precursors and/or erythroid cells; in supporting the growth and proliferation of myeloid cells such as granulocytes and monocytes/macrophages (i.e., traditional CSF activity) 5 useful, for example, in conjunction with chemotherapy to prevent or treat consequent myelo-suppression; in supporting the growth and proliferation of megakaryocytes and consequently of platelets thereby allowing prevention or treatment of various platelet disorders such as 10 thrombocytopenia, and generally for use in place of or complimentary to platelet transfusions; and/or in supporting the growth and proliferation of hematopoietic stem cells which are capable of maturing to any and all of the above-mentioned hematopoietic cells and therefore find therapeutic 15 utility in various stem cell disorders (such as those usually treated with transplantation, including, without limitation, aplastic anemia and paroxysmal nocturnal hemoglobinuria), as well as in repopulating the stem cell compartment post irradiation/chemotherapy, either in-vivo or 20 ex-vivo (i.e., in conjunction with bone marrow transplantation or with peripheral progenitor cell transplantation (homologous or heterologous)) as normal cells or genetically manipulated for gene therapy.

The activity of a protein of the invention may, among 25 other means, be measured by the following methods:

Suitable assays for proliferation and differentiation of various hematopoietic lines are cited above.

Assays for embryonic stem cell differentiation (which will identify, among others, proteins that influence 30 embryonic differentiation hematopoiesis) include, without limitation, those described in: Johansson et al. Cellular Biology 15:141-151, 1995; Keller et al., Molecular and

Cellular Biology 13:473-486, 1993; McClanahan et al., Blood 81:2903-2915, 1993.

Assays for stem cell survival and differentiation (which will identify, among others, proteins that regulate lympho-hematopoiesis) include, without limitation, those described in: Methylcellulose colony forming assays, Freshney, M.G. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 265-268, Wiley-Liss, Inc., New York, NY. 1994; Hirayama et al., Proc. Natl. Acad. Sci. USA 89:5907-5911, 1992; Primitive hematopoietic colony forming cells with high proliferative potential, McNiece, I.K. and Briddell, R.A. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 23-39, Wiley-Liss, Inc., New York, NY. 1994; Neben et al., Experimental Hematology 22:353-359, 1994; Cobblestone area forming cell assay, Ploemacher, R.E. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 1-21, Wiley-Liss, Inc., New York, NY. 1994; Long term bone marrow cultures in the presence of stromal cells, Spooncer, E., Dexter, M. and Allen, T. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 163-179, Wiley-Liss, Inc., New York, NY. 1994; Long term culture initiating cell assay, Sutherland, H.J. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 139-162, Wiley-Liss, Inc., New York, NY. 1994.

25 Tissue Growth Activity

A protein of the present invention also may have utility in compositions used for bone, cartilage, tendon, ligament and/or nerve tissue growth or regeneration, as well as for wound healing and tissue repair and replacement, and in the treatment of burns, incisions and ulcers.

A protein of the present invention, which induces cartilage and/or bone growth in circumstances where bone is

not normally formed, has application in the healing of bone fractures and cartilage damage or defects in humans and other animals. Such a preparation employing a protein of the invention may have prophylactic use in closed as well as open fracture reduction and also in the improved fixation of artificial joints. De novo bone formation induced by an osteogenic agent contributes to the repair of congenital, trauma induced, or oncologic resection induced craniofacial defects, and also is useful in cosmetic plastic surgery.

A protein of this invention may also be used in the treatment of periodontal disease, and in other tooth repair processes. Such agents may provide an environment to attract bone-forming cells, stimulate growth of bone-forming cells or induce differentiation of progenitors of bone-forming cells. A protein of the invention may also be useful in the treatment of osteoporosis or osteoarthritis, such as through stimulation of bone and/or cartilage repair or by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes.

Another category of tissue regeneration activity that may be attributable to the protein of the present invention is tendon/ligament formation. A protein of the present invention, which induces tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and other animals. Such a preparation employing a tendon/ligament-like tissue inducing protein may have prophylactic use in preventing damage to tendon or ligament tissue, as well as use in the improved fixation of tendon or ligament to bone or other tissues, and

trauma and cerebrovascular diseases such as stroke. Peripheral neuropathies resulting from chemotherapy or other medical therapies may also be treatable using a protein of the invention.

5 Proteins of the invention may also be useful to promote better or faster closure of non-healing wounds, including without limitation pressure ulcers, ulcers associated with vascular insufficiency, surgical and traumatic wounds, and the like.

10 It is expected that a protein of the present invention may also exhibit activity for generation or regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac) and vascular (including
15 vascular endothelium) tissue, or for promoting the growth of cells comprising such tissues. Part of the desired effects may be by inhibition or modulation of fibrotic scarring to allow normal tissue to regenerate. A protein of the invention may also exhibit angiogenic activity.

20 A protein of the present invention may also be useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokine damage.

25 A protein of the present invention may also be useful for promoting or inhibiting differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

The activity of a protein of the invention may, among other means, be measured by the following methods:

30 Assays for tissue generation activity include, without limitation, those described in: International Patent Publication No. WO95/16035 (bone, cartilage, tendon);

International Patent Publication No. WO95/05846 (nerve, neuronal); International Patent Publication No. WO91/07491 (skin, endothelium).

5 Assays for wound healing activity include, without limitation, those described in: Winter, Epidermal Wound Healing, pps. 71-112 (Maibach, HI and Rovee, DT, eds.), Year Book Medical Publishers, Inc., Chicago, as modified by Eaglstein and Mertz, J. Invest. Dermatol 71:382-84 (1978).

Activin/Inhibin Activity

10 A protein of the present invention may also exhibit activin- or inhibin-related activities. Inhibins are characterized by their ability to inhibit the release of follicle stimulating hormone (FSH), while activins and are
15 characterized by their ability to stimulate the release of follicle stimulating hormone (FSH). Thus, a protein of the present invention, alone or in heterodimers with a member of the inhibin family, may be useful as a contraceptive based on the ability of inhibins to decrease fertility in female mammals and decrease spermatogenesis in male mammals.
20 Administration of sufficient amounts of other inhibins can induce infertility in these mammals. Alternatively, the protein of the invention, as a homodimer or as a heterodimer with other protein subunits of the inhibin- group, may be useful as a fertility inducing therapeutic, based upon the
25 ability of activin molecules in stimulating FSH release from cells of the anterior pituitary. See, for example, United States Patent 4,798,885. A protein of the invention may also be useful for advancement of the onset of fertility in sexually immature mammals, so as to increase the lifetime
30 reproductive performance of domestic animals such as cows, sheep and pigs.

The activity of a protein of the invention may, among

other means, be measured by the following methods:

Assays for activin/inhibin activity include, without limitation, those described in: Vale et al., Endocrinology 91:562-572, 1972; Ling et al., Nature 321:779-782, 1986; 5 Vale et al., Nature 321:776-779, 1986; Mason et al., Nature 318:659-663, 1985; Forage et al., Proc. Natl. Acad. Sci. USA 83:3091-3095, 1986.

Chemotactic/Chemokinetic Activity

10 A protein of the present invention may have chemotactic or chemokinetic activity (e.g., act as a chemokine) for mammalian cells, including, for example, monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells. Chemotactic and chemokinetic proteins can be used to mobilize or attract a 15 desired cell population to a desired site of action. Chemotactic or chemokinetic proteins provide particular advantages in treatment of wounds and other trauma to tissues, as well as in treatment of localized infections. For example, attraction of lymphocytes, monocytes or 20 neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

A protein or peptide has chemotactic activity for a particular cell population if it can stimulate, directly or 25 indirectly, the directed orientation or movement of such cell population. Preferably, the protein or peptide has the ability to directly stimulate directed movement of cells. Whether a particular protein has chemotactic activity for a population of cells can be readily determined by employing 30 such protein or peptide in any known assay for cell chemotaxis.

The activity of a protein of the invention may, among

other means, be measured by the following methods:

Assays for chemotactic activity (which will identify proteins that induce or prevent chemotaxis) consist of assays that measure the ability of a protein to induce the migration of cells across a membrane as well as the ability of a protein to induce the adhesion of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 6.12, Measurement of alpha and beta Chemokines 6.12.1-6.12.28; Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al. APMIS 103:140-146, 1995; Muller et al Eur. J. Immunol. 25: 1744-1748; Gruber et al. J. of Immunol. 152:5860-5867, 1994; Johnston et al. J. of Immunol. 153: 1762-1768, 1994.

Hemostatic and Thrombolytic Activity

A protein of the invention may also exhibit hemostatic or thrombolytic activity. As a result, such a protein is expected to be useful in treatment of various coagulation disorders (including hereditary disorders, such as hemophilias) or to enhance coagulation and other hemostatic events in treating wounds resulting from trauma, surgery or other causes. A protein of the invention may also be useful for dissolving or inhibiting formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as, for example, infarction of cardiac and central nervous system vessels (e.g., stroke)).

30 The activity of a protein of the invention may, among other means, be measured by the following methods:

Assay for hemostatic and thrombolytic activity include,

Suitable assays for receptor-ligand activity include without limitation those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 7.28, Measurement of Cellular Adhesion under static conditions 7.28.1-7.28.22),

Takai et al., Proc. Natl. Acad. Sci. USA 84:6864-6868, 1987; Bierer et al., J. Exp. Med. 168:1145-1156, 1988; Rosenstein et al., J. Exp. Med. 169:149-160 1989; Stoltenborg et al., J. Immunol. Methods 175:59-68, 1994; Stitt et al.,
5 Cell 80:661-670, 1995.

Anti-Inflammatory Activity

Proteins of the present invention may also exhibit anti-inflammatory activity. The anti-inflammatory activity may be achieved by providing a stimulus to cells involved in
10 the inflammatory response, by inhibiting or promoting cell-cell interactions (such as, for example, cell adhesion), by inhibiting or promoting chemotaxis of cells involved in the inflammatory process, inhibiting or promoting cell
15 extravasation, or by stimulating or suppressing production of other factors which more directly inhibit or promote an inflammatory response. Proteins exhibiting such activities can be used to treat inflammatory conditions including
20 chronic or acute conditions), including without limitation inflammation associated with infection (such as septic shock, sepsis or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine or chemokine-induced lung injury, inflammatory
25 bowel disease, Crohn's disease or resulting from over production of cytokines such as TNF or IL-1. Proteins of the invention may also be useful to treat anaphylaxis and hypersensitivity to an antigenic substance or material.

Tumor Inhibition Activity

In addition to the activities described above for
30 immunological treatment or prevention of tumors, a protein of the invention may exhibit other anti-tumor activities. A

protein may inhibit tumor growth directly or indirectly (such as, for example, via ADCC). A protein may exhibit its tumor inhibitory activity by acting on tumor tissue or tumor precursor tissue, by inhibiting formation of tissues necessary to support tumor growth (such as, for example, by inhibiting angiogenesis), by causing production of other factors, agents or cell types which inhibit tumor growth, or by suppressing, eliminating or inhibiting factors, agents or cell types which promote tumor growth

10 Other Activities

A protein of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria, viruses, fungi and other parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, weight, hair color, eye color, skin, fat to lean ratio or other tissue pigmentation, or organ or body part size or shape (such as, for example, breast augmentation or diminution, change in bone form or shape); effecting biorhythms or circadian cycles or rhythms; effecting the fertility of male or female subjects; effecting the metabolism, catabolism, anabolism, processing, utilization, storage or elimination of dietary fat, lipid, protein, carbohydrate, vitamins, minerals, cofactors or other nutritional factors or component(s); effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), depression (including depressive disorders) and violent behaviors; providing analgesic effects or other pain reducing effects; promoting differentiation and growth of

embryonic stem cells in lineages other than hematopoietic lineages; hormonal or endocrine activity; in the case of enzymes, correcting deficiencies of the enzyme and treating deficiency-related diseases; treatment of hyperproliferative disorders (such as, for example, psoriasis); immunoglobulin-like activity (such as, for example, the ability to bind antigens or complement); and the ability to act as an antigen in a vaccine composition to raise an immune response against such protein or another material or entity which is cross-reactive with such protein.

Examples

The present invention is specifically illustrated in more detail by the following Examples, but Examples are not intended to restrict the present invention. The basic operations with regard to the recombinant DNA and the enzymatic reactions were carried out according to the literature ["Molecular Cloning. A Laboratory Manual", Cold Spring Harbor Laboratory, 1989]. Unless otherwise stated, restrictive enzymes and a variety of modification enzymes to be used were those available from Takara Shuzo. The buffer compositions and the reaction conditions for each of the enzyme reactions were as described in the manufacturer's instructions. The cDNA synthesis was carried out according to the literature [Kato, S. et al., Gene 150: 243-250 (1994)].

(1) Selection of cDNAs Encoding Proteins Having Hydrophobic Domains

The cDNA library of fibrosarcoma cell line HT-1080 (WO98/11217), the cDNA library of osteosarcoma cell line Saos-2 (WO97/33993), the cDNA library of osteosarcoma cell line U-2 OS (WO98/21328), the cDNA library of epidermoid

carcinoma cell line KB (WO98/11217), the cDNA library of tissues of stomach cancer delivered by the operation (WO98/21328), the cDNA library of liver tissue delivered by the operation (WO98/21328), and were used for the cDNA
5 libraries. Full-length cDNA clones were selected from respective libraries and the whole base sequences thereof were determined to construct a homo-protein cDNA bank consisting of the full-length cDNA clones. The hydrophobicity/hydrophilicity profiles were determined for
10 the proteins encoded by the full-length cDNA clones registered in the homo-protein cDNA bank by the Kyte-Doolittle method [Kyte, J. & Doolittle, R. F., J. Mol. Biol. 157: 105-132 (1982)] to examine the presence or absence of a hydrophobic region. Any clone that has a hydrophobic region
15 being putative as a secretory signal or a transmembrane domain in the amino acid sequence of the encoded protein was selected as a clone candidate.

(2) Protein Synthesis by In Vitro Translation

The plasmid vector bearing the cDNA of the present
20 invention was used for in vitro transcription/translation with a T_NT rabbit reticulocyte lysate kit (Promega). In this case, [³⁵S]methionine was added to label the expression product with a radioisotope. Each of the reactions was carried out according to the protocols attached to the kit.
25 Two micrograms of the plasmid was subjected to the reaction at 30°C for 90 minutes in the reaction solution of a total volume of 25 µl containing 12.5 µl µ of T_NT rabbit reticulocyte lysate, 0.5 µl of a buffer solution (attached to the kit), 2 µl of an amino acid mixture (without
30 methionine), 2 µl of [³⁵S]methionine (Amersham) (0.37 MBq/µl), 0.5 µl of T7 RNA polymerase, and 20 U of RNasin. Also, an experiment in the presence of a membrane system was carried

out by adding to this reaction system 2.5 μ l of a canine pancreas microsome fraction (Promega). To 3 μ l of the resulting reaction solution was added 2 μ l of the SDS sampling buffer (125 mM Tris-hydrochloric acid buffer, pH 6.8, 120 mM 2-mercaptoethanol, 2% SDS solution, 0.025% bromophenol blue, and 20% glycerol) and the resulting mixture was heated at 95°C for 3 minutes and then subjected to SDS-polyacrylamide gel electrophoresis. The molecular weight of the translation product was determined by carrying out the autoradiography.

(3) Expression by COS7

Escherichia coli cells bearing the expression vector for the protein of the present invention was incubated at 37°C for 2 hours in 2 ml of the 2xYT culture medium containing 100 μ g/ml of ampicillin, the helper phage M13KO7 (50 μ l) was added, and the incubation was continued at 37°C overnight. A supernatant separated by centrifugation underwent precipitation with polyethylene glycol to obtain single-stranded phage particles. These particles were suspended in 100 μ l of 1 mM Tris-0.1 mM EDTA, pH 8 (TE).

The cultured cells derived from simian kidney, COS7, were incubated at 37°C in the presence of 5% CO₂ in the Dulbecco's modified Eagle's culture medium (DMEM) containing 10% fetal calf serum. Into a 6-well plate (Nunc, well diameter: 3 cm) were inoculated with 1 x 10⁵ COS7 cells and incubation was carried out at 37°C for 22 hours in the presence of 5% CO₂. After the culture medium was removed, the cell surface was washed with a phosphate buffer solution and then washed again with DMEM containing 50 mM Tris-hydrochloric acid (pH 7.5) (TDMEM). To the resulting cells was added a suspension of 1 μ l of the single-stranded phage suspension, 0.6 ml of the DMEM culture medium, and 3 μ l of

TRANSFECTAM™ (IBF) and the resulting mixture was incubated at 37°C for 3 hours in the presence of 5% CO₂. After the sample solution was removed, the cell surface was washed with TDMEM, 2 ml per well of DMEM containing 10% fetal calf serum was added, and the incubation was carried out at 37°C for 2 days in the presence of 5% CO₂. After the culture medium was replaced by a culture medium containing [³⁵S]cystine or [³⁵S]methionine, the incubation was carried out for one hour. After the culture medium and the cells were separated by centrifugation, proteins in the culture medium fraction and the cell-membrane fraction were subjected to SDS-PAGE.

(4) Clone Examples

<HP01550> (SEQ ID Nos. 1, 11, and 21)

Determination of the whole base sequence of the cDNA insert of clone HP01550 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 65-bp 5'-untranslated region, a 378-bp ORF, and a 67-bp 3'-untranslated region. The ORF codes for a protein consisting of 125 amino acid residues and there existed one putative transmembrane domain. Figure 1 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 15 kDa that was almost identical with the molecular weight of 13,825 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein F45G2.c (GenBank Accession No. Z93382). Table 2 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the C.

Determination of the whole base sequence of the cDNA insert of clone HP02593 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 103-bp 5'-untranslated region, a 396-bp ORF,

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA306490) in ESTs, but, since they
5 are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10195> (SEQ ID Nos. 3, 13, and 23)

10 Determination of the whole base sequence of the cDNA insert of clone HP10195 obtained from cDNA library of human fibrosarcoma HT-1080 revealed the structure consisting of a 286-bp 5'-untranslated region, a 729-bp ORF, and a 604-bp
15 3'-untranslated region. The ORF codes for a protein consisting of 242 amino acid residues and there existed one putative transmembrane domain at the C-terminus. Figure 3 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In
20 vitro translation resulted in formation of a translation product of 32 kDa that was somewhat larger than the molecular weight of 27,300 predicted from the ORF. When expressed in COS7 cells, an expression product of about 21 kDa was observed in the supernatant fraction and the
25 membrane fraction.

25 The search of the protein data base using the amino acid sequence of the present protein has revealed the registration of sequences that were similar to the Aplysia VAP-33 (SWISS-PROT Accession No. P53173). Table 4 shows the
30 comparison between amino acid sequences of the human protein of the present invention (HP) and the Aplysia VAP-33 (AP). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the

Determination of the whole base sequence of the cDNA insert of clone HP10423 obtained from cDNA library of human osteosarcoma cell line U-2 OS revealed the structure consisting of a 64-bp 5'-untranslated region, a 795-bp ORF, and a 207-bp 3'-untranslated region. The ORF codes for a protein consisting of 264 amino acid residues and there existed a secretory signal at the N-terminus and one putative transmembrane domain at the N-terminus. Figure 4 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 30 kDa that was almost identical with the molecular weight of 29,377 predicted from the ORF. When expressed in COS7 cells, an expression product of about 31 kDa was observed in the membrane fraction.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. D80116) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10506> (SEQ ID Nos. 5, 15, and 25)

Determination of the whole base sequence of the cDNA insert of clone HP10506 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 53-bp 5'-untranslated region, a 339-bp ORF, and a 226-bp 3'-untranslated region. The ORF codes for a protein consisting of 112 amino acid residues and there existed one putative transmembrane domain. Figure 5 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-

Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 11,821 predicted from the ORF. When expressed in COS7 cells, an expression product of about 13 kDa was observed in the membrane fraction.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA282544) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10507> (SEQ ID Nos. 6, 16, and 26)

Determination of the whole base sequence of the cDNA insert of clone HP10507 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 412-bp 5'-untranslated region, a 441-bp ORF, and a 168-bp 3'-untranslated region. The ORF codes for a protein consisting of 146 amino acid residues and there existed a secretory signal at the N-terminus and one putative transmembrane domain at the C-terminus. Figure 6 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 19 kDa that was somewhat larger than the molecular weight of 16,347 predicted from the ORF.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA424759) in ESTs, but, since they

are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

5 <HP10548> (SEQ ID Nos. 7, 17, and 27)

Determination of the whole base sequence of the cDNA insert of clone HP10548 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 330-bp 5'-untranslated region, a 1035-bp ORF, and a 67-bp 3'-
10 untranslated region. The ORF codes for a protein consisting of 344 amino acid residues and there existed four putative transmembrane domains. Figure 7 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro
15 translation resulted in formation of a translation product of a high molecular weight.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for
20 example, Accession No. AA143152) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

25 <HP10566> (SEQ ID Nos. 8, 18, and 28)

Determination of the whole base sequence of the cDNA insert of clone HP10566 obtained from cDNA library of the human stomach cancer revealed the structure consisting of a 61-bp 5'-untranslated region, a 294-bp ORF, and a 246-bp 3'-
30 untranslated region. The ORF codes for a protein consisting of 97 amino acid residues and there existed one putative transmembrane domain at the C-terminus. Figure 8 depicts the

Furthermore, the search of the GenBank using the base
30 sequences of the present cDNA has revealed the registration
of sequences that shared a homology of 90% or more (for
example, Accession No. AA428475) in ESTs, but, since they

are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

5 <HP10568> (SEQ ID Nos. 10, 20, and 30)

Determination of the whole base sequence of the cDNA insert of clone HP10568 obtained from cDNA library of the human stomach cancer revealed the structure consisting of a 56-bp 5'-untranslated region, a 984-bp ORF, and a 60-bp 3'-untranslated region. The ORF codes for a protein consisting of 327 amino acid residues and there existed a secretory signal at the N-terminus and one putative transmembrane domain at the C-terminus. Figure 10 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 36.5 kDa that was almost identical with the molecular weight of 34,326 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 40 kDa which is considered to have a sugar chain being attached. In addition, there exist in the amino acid sequence of this protein two sites at which N-glycosylation may occur (Asn-Leu-Thr at position 138 and Asn-Leu-Ser at position 206). Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from valine at position 24. When expressed in COS7 cells, an expression product of about 31 kDa was observed in the supernatant fraction and the membrane fraction.

30 The search of the protein data base using the amino acid sequence of the present protein has revealed that the protein was similar to the human cell-surface A33 antigen

(SWISS-PROT Accession No. Q99795). Table 5 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human cell-surface A33 antigen (A3). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 30.0% in the N-terminal region of 243 residues.

Table 5

	HP	MAELPGPFLLCGALLGFLCLSGLAWEVKVPTEPLSTPLGKTAELTCTYSTSVGDSFAL-EW	
		*.....*
15	A3	MVGKMWPVLWTLCAVRVTVDAISVETPQDVLRASQGKSVTLPCITYHTSTSSREGLIQW	
	HP	SFVQPGKPISESHPILYFTNGHLYPTGSKSKRVSLQNPPTVGVATLKLTDVHPSDGTGY	
		*.....*
	A3	DKLL--LTHTERVVIWPFSSNKN-YIHGELYKNRVSISSNAEQSDASITIDQLTMADNGTY	
	HP	LCQVNNPPDFYTNGLGLINLTVLVPPSNPLCSQSGQTSVGGSTALRCSSEGAPKPVYNW	
20		*	*.....*
	A3	ECSVSLMSDLEGNTKSRVRLVLVPPSKPECGIEGETIIGNNIQLTCQSKEGSPTPQYSW	
	HP	VRLGTFPTPSPGSMVQDEVSGQLILTNLSLTSSGTYRCVATNQMGASCELTLSVTEPS-	
		*	*.....*
	A3	KRYNILNOEOP--LAQPASGQPVSLKNISTDTSGYYICTSSNEEGTQFCNITVAVRSPSM	
25	HP	-QGRVAGALIGVLLGVLLLSVAAFCLVRVQKRGKKPKETYGGSDLREDAIAPGISHTTC	
		. . *	
	A3	NVALYVGIAVGVAALIIIGIIIIYCCCCRGKDDNTEDKEDARPNREAYEEPPEQLRSLR	
	HP	MRADSSKGFLERPSSASTVTTTSSKLPMVV	
30	A3	EREEEDDYRQEEQRSTGRESFDHLDQ	

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration

of sequences that shared a homology of 90% or more (for example, Accession No. T24595) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein
5 of the present invention.

<HP01426> (SEQ ID Nos. 31, 41, and 51)

Determination of the whole base sequence of the cDNA insert of clone HP01426 obtained from cDNA library of human
10 stomach cancer revealed the structure consisting of a 1-bp 5'-untranslated region, a 942-bp ORF, and a 122-bp 3'-untranslated region. The ORF codes for a protein consisting of 313 amino acid residues and there existed a putative secretory signal. Figure 11 depicts the
15 hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 36 kDa that was almost identical with the molecular weight of 34,955 predicted from the ORF. In this case, the
20 addition of a microsome led to the formation of a product of 38 kDa which is considered to have a sugar chain being attached after secretion. In addition, there exists in the amino acid sequence of this protein one site at which N-glycosylation may occur (Asn-Ser-Ser at position 163).
25 Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from tryptophan at position 17. When expressed in COS7 cells, an expression product of about 39 kDa was observed in the supernatant
30 fraction and the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the

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15 HP MNQLSFLFLFIATTRGWSTDEANTYFKWEWTCSSSPSLPRSCKEIKDECPSAFDGLYFLRT
    *          **                      *          *****. . * ** * *
XL MLVHILLLLLVTTGGLSQSCEPVVIVASKNMVKQLDCDKFRSCKEIKDSNEEAQDGIYTLTS
HP ENGVIIYQTFCDMTSGGGGWTLVASVHENDMRGKCTVGDRWSSQQGSKADYPEGDGNWANY
    . . * . ***** . ***** . * **** . ***** . *****
XL SDGISYQTFCDMTTNGGGWTLVASVHENNMAGKCTIGDRWSSQQGNRADYPEGDGNWANY
20 HP NTFGSAEAATSDDYKNPGYYDIQAKDLGIWHVPNKSPMQHWRNSSLLRYRTDTGFLQTLG
    ***** . ***** . * . ** . ***** . ***** ***** . * . *
XL NTFGSAGGATSDDYKNPGYYDIEAYNLGVHVPNKTPLSVWRNSSLQRYRTTDGILFKHG
HP HNLFGIYQKYPVKYGEKGCWTDNGPVI PVVYDFGDAQKTASYYSPIYGQREFTAGFVQFRV
    *** . . * . ***** * . * . * . ***** . * . * . *** . *** . . . ** . * . ***
25 XL GNLFSLYRIYPVKYGIGSCSKDSGPTVPVVDLGSAKLTASFYSPDFRSQFTPGYIQFRP
HP FNNERAANALCAGMRVTGCNTEHHCIGGGYFPEAS PQCGDFSGFDWSGYGTHVGYSSE
    . * . * . ** *** . ** . . . * . ** ***** . * . ***** . . . * . ***** . * .
XL INTEKAALALCPGMKMESCNVEHVCIGGGYFPEADPRQCGDFAAYDFNGYGTKKFNSAG
HP REITEAAVLLFYR
    *****
30 XL IEITEAAVLLFYL

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<HP02515> (SEQ ID Nos. 32, 42, and 52)

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<HP02575> (SEQ ID Nos. 33, 43, and 53)

Determination of the whole base sequence of the cDNA insert of clone HP02575 obtained from cDNA library of human osteosarcome cell line Saos-2 revealed the structure consisting of a 55-bp 5'-untranslated region, a 1404-bp ORF, and a 219-bp 3'-untranslated region. The ORF codes for a protein consisting of 467 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 13 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 52 kDa that was almost identical with the molecular weight of 54,065 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 57 kDa which is considered to have a sugar chain being attached afetr secretion. In addition, there exist in the amino acid sequence of this protein three sites at which N-glycosylation may occur (Asn-Arg-Thr at position 171, Asn-Ser-Thr at position 239 and Asn-Asp-Thr at position 377). Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from histidine at position 29. When expressed in COS7 cells, an expression product of about 55 kDa was observed in the supernatant fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human α -L-fucosidase (SWISS-PROT Accession No. P04066). Table 8 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human α -L-fucosidase (FC). Therein,

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. N28668) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

10 <HP10357> (SEQ ID Nos. 34, 44, and 54)

Determination of the whole base sequence of the cDNA insert of clone HP10357 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 113-bp 5'-untranslated region, a 300-bp ORF, and a 54-bp 3'-untranslated region. The ORF codes for a protein consisting of 99 amino acid residues and there existed two putative transmembrane domains. Figure 14 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 11 kDa that was almost identical with the molecular weight of 10,923 predicted from the ORF.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA477156) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

30

<HP10447> (SEQ ID Nos. 35, 45, and 55)

Determination of the whole base sequence of the cDNA

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA420715) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10557> (SEQ ID Nos. 39, 49, and 59)

Determination of the whole base sequence of the cDNA insert of clone HP10557 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 24-bp 5'-untranslated region, a 519-bp ORF, and a 130-bp 3'-untranslated region. The ORF codes for a protein consisting of 172 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 19 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 32 kDa that was larger than the molecular weight of 18,844 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 39 kDa which is considered to have been subjected to some modification after secretion. In addition, there exist in the amino acid sequence of this protein no site at which N-glycosylation may occur. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glycine at position 32. When expressed in COS7 cells, an expression product of about 20 kDa was observed in the supernatant fraction and the membrane fraction.

example, Accession No. AA101709) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP10563> (SEQ ID Nos. 40, 50, and 60)

Determination of the whole base sequence of the cDNA insert of clone HP10563 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure
10 consisting of a 126-bp 5'-untranslated region, a 363-bp ORF, and a 936-bp 3'-untranslated region. The ORF codes for a protein consisting of 120 amino acid residues and there existed two putative transmembrane domains. Figure 20 depicts the hydrophobicity/hydrophilicity profile, obtained
15 by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 18.5 kDa that was larger than the molecular weight of 13,180 predicted from the ORF.

The search of the protein data base using the amino
20 acid sequence of the present protein revealed that the protein was similar to the Arabidopsis thaliana hypothetical protein F27F23.15 (GenBank Accession No. AC003058). Table 13 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the A.
25 thaliana hypothetical protein F27F23.15 (AT). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins
30 shared a homology of 35.5% in the entire region.

Table 13

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HP MMPSRTNLATGIPSSKVYSRLSSTDDGYIDLQFKKTPPKIPYKAIALATVLFLIGAFLI
      *...* *. . . . . * *...*. *...*. *
5  AT      MAYVDHAFSISDEDLMIGTSY-TVSNRPPVKEISLAVGLLVFGTLGI
HP IIGSLLLSGYISKGGADRAVPVLIIGILVFLPGFYHLRIAYYASKGYRGYSYDDIPDFDD
      ..* .. . . . *. . . . . . . *...*. *...*. *...*. *...*. *
AT VLGFFMAYNRVG-GDRGHGIFIVLGCLLFIPGFYYTRIAYYAYKGYKGFSFSNIPSV

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA083574) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP01467> (SEQ ID Nos. 61, 71, and 81)

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Determination of the whole base sequence of the cDNA insert of clone HP01467 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 65-bp 5'-untranslated region, a 924-bp ORF, and a 447-bp 3'-untranslated region. The ORF codes for a protein consisting of 307 amino acid residues and there existed three putative transmembrane domains. Figure 21 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

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The search of the protein data base using the amino

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA421925) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP01956> (SEQ ID Nos. 62, 72, and 82)

Determination of the whole base sequence of the cDNA insert of clone HP01956 obtained from cDNA library of human liver revealed the structure consisting of a 86-bp 5'-untranslated region, a 552-bp ORF, and a 359-bp 3'-untranslated region. The ORF codes for a protein consisting of 183 amino acid residues and there existed one putative transmembrane domain. Figure 22 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 20.5 kDa that was almost identical with the molecular weight of 20,073 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the yeast hypothetical protein 21.5 kDa (SWISS-PROT Accession No. P53073). Table 15 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the yeast hypothetical protein 21.5 kDa (SC). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology

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Determination of the whole base sequence of the cDNA
30 insert of clone HP02631 obtained from cDNA library of human
osteosarcoma cell line Saos-2 revealed the structure
consisting of a 42-bp 5'-untranslated region, a 147-bp ORF,

and a 1191-bp 3'-untranslated region. The ORF codes for a protein consisting of 48 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 25 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 10 kDa or less.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA156969) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02632> (SEQ ID Nos. 66, 76, and 86)

Determination of the whole base sequence of the cDNA insert of clone HP02632 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 50-bp 5'-untranslated region, a 1116-bp ORF, and a 337-bp 3'-untranslated region. The ORF codes for a protein consisting of 371 amino acid residues and there existed eight putative transmembrane domains. Figure 26 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein CELC2H12 (GenBank Accession No. U23169). Table 18 shows the comparison between amino acid sequences

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Table 19

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HP  MVDRGPLLTSAlIFYLAIGAAIFEVLEEPHWKEAKKNYYTQKLHLLKEFPCLGQEGLDK
      * . ...** . ** .....** ..*.*. . ....**.....
5  MM  MRSTLLALLALVLLYLVS GALVFQALEQPHEQQAQKKMDHGRDQFLRDHPCVSQKSLED
HP  ILEVVS DAAGQG-----VAITGNQTFNNWNWPNAMIFAATVITTIGYGNVAPKTPAGRLF
      ..... * * * ..... ** .....*****.. * *****
MM  FIKLLVEALGGGANPETS WTNSSNHSSAWNLGSAFFFSGTIITTIGYGNIVLHTDAGRLE
HP  CVFYGLFGVPLCLTWISALGKFFGGRAKR----LGQFLTKRGVSLRKAQITCTVIFIVWG
10  *.*.* *.* * .....* .....* .....*.* .. ..*.*.* *
MM  CIFYALVGIPFLFGMLLAGVGDRLGSSLRRGIGHIEAIFLKWHPGLVRSLSAVLFLIG
HP  VLVHLVIPPFVFMVTEGWN YIEGLYYSFITISTIGFGDFVAGVNPSANYHALYRYFVELW
      *. ....** *.* .....*****.* * .....*.* *
MM  CLLFVLTPTFVFSYMESWSKLEAIYFVIVTLTTVGFGDYVPG-DGTGQNSPAYQPLVWFW
15  HP  IYLGLAWLSLFVNWKVSMFVEVHKAIKRRRRRRKESFESSPHSRKALQVKGSTASKDVNI
      * .....
MM  ILFGLAYFASVLT TIGNWLRAVSRRTAEMGGLTAQAASWTGTVTARVTQRTGPSAPPPE

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20 Furthermore, the search of the GenBank using the base
sequences of the present cDNA has revealed the registration
of sequences that shared a homology of 90% or more (for
example, Accession No. R25184) in ESTs, but, since they are
partial sequences, it can not be judged whether or not any
25 of these sequences codes for the same protein as the protein
of the present invention.

<HP10542> (SEQ ID Nos. 69, 79, and 89)

30 Determination of the whole base sequence of the cDNA
insert of clone HP10542 obtained from cDNA library of human
stomach cancer revealed the structure consisting of a 23-bp
5'-untranslated region, a 321-bp ORF, and a 426-bp 3'-

untranslated region. The ORF codes for a protein consisting of 106 amino acid residues and there existed one putative transmembrane domain. Figure 29 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 11,724 predicted from the ORF. When expressed in COS7 cells, an expression product of about 13 kDa was observed in the membrane fraction.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA029683) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10571> (SEQ ID Nos. 70, 80, and 90)

Determination of the whole base sequence of the cDNA insert of clone HP10571 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 95-bp 5'-untranslated region, a 459-bp ORF, and a 675-bp 3'-untranslated region. The ORF codes for a protein consisting of 152 amino acid residues and there existed one putative transmembrane domain. Figure 30 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 20 kDa that was larger than the molecular weight of 17,062 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 23 kDa

Determination of the whole base sequence of the cDNA insert of clone HP01470 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 157-bp 5'-untranslated region, a 1077-bp ORF, and a 385-bp 3'-untranslated region. The ORF codes for a protein consisting of 358 amino acid residues and there existed one putative transmembrane domain. Figure 31 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 43 kDa that was somewhat larger than the molecular weight of 40,489 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 40 kDa from which the secretory signal is considered to have been cleaved and a product of 43.5 kDa which is considered to have been subjected to some modification. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glycine at position 23. When

expressed in COS7 cells, an expression product of about 44 kDa was observed in the supernatant fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein 39.9 kDa (SWISS-PROT Accession No. Q10005). Table 20 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein 39.9 kDa (CE). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 58.9% in the entire region.

Determination of the whole base sequence of the cDNA insert of clone HP02419 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 253-bp

5'-untranslated region, a 681-bp ORF, and a 1120-bp 3'-untranslated region. The ORF codes for a protein consisting of 226 amino acid residues and there existed four putative transmembrane domains. Figure 32 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human hypothetical protein KIAA0108 (SWISS-PROT Accession No. Q15012). Table 21 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human hypothetical protein KIAA0108 (KI). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 43.9% in the entire region.

Determination of the whole base sequence of the cDNA insert of clone HP02631 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 42-bp 5'-untranslated region, a 588-bp ORF, and a 750-bp 3'-untranslated region. Although the 49th amino acid residue is encoded by a stop codon, it is likely that this codon encodes selenocysteine from the molecular weight

of the translation product and the sequence comparison data with the *Caenorhabditis elegans* homologue. The ORF codes for a protein consisting of 195 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain in the intermediate region. Figure 33 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 58 kDa. In this case, the addition of a microsome led to the formation of a product of 56 kDa from which the secretory signal is considered to have been cleaved. Since both of these products are larger than the molecular weight of 22 kDa predicted from the ORF, it is likely that the protein interacts with another protein.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein C35C5.3 (EMBL Accession No. Z78417). Table 22 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein C35C5.3 (CE). U at position 49 in the amino acid sequence of the protein of the present invention represents selenocysteine. Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 37.9% in the entire region other than the N-terminal region. Cystein was found in the sequence of the *C. elegans* protein at the position corresponding to position 49 encoded by the stop codon (selenocysteine) of the protein of the present invention.

Table 22

	HP	MRLLLL
5	CE MRIHDELQKQDMSRFGVFIIGVLFFMSVCDVLRTEESHSHDENHVHEKDDFEAEFGDETDS	
	HP LLVAASAMVRSEASANLGGVPSKRLKMQYATGPLLKQICVSUGYRRVFEEYMRVISQRY	
		* *.. *** *...*... ..*
	CE QSFSQGTEEDHIEVREQSSFVKPTAVVHAKDLPTLRIFYCVSCGYKQAFDQFTTFAKEY	
	HP PDIRIEGENYLPQPIYRHIAFSLSVFKLVLIIGLVKDPFAFFGMQAPS IWQWGQENKV	
10	*...***.*. * ..* ** *... *.. * .***. **. * * * ..***.	
	CE PNMPIEGANFAPVLWKAYVAQALS FVKMAVLVLVLGGINPFERFGLGYPQILQHAHGNKM	
	HP YACMMVFFLSNMIENQCMSTGA FEITLNDVPVWSKLESGHLPSMQQLVQILDNEMKLVNH	
		.***.***.*...*. *****. *.. ..****.***** *...*...*... .
	CE SSCMLVFMLGNLVEQSLISTGA FEVYLGNEQIWSKIESGRVPSPQEFMQLIDAQLAVLGK	
15	HP MDSIPHRS	
	CE APVNTESFGEFQQTV	

20 Furthermore, the search of the GenBank using the base
sequences of the present cDNA has revealed the registration
of sequences that shared a homology of 90% or more (for
example, Accession No. AA156969) in ESTs, but, since they
are partial sequences, it can not be judged whether or not
25 any of these sequences codes for the same protein as the
protein of the present invention.

<HP02695> (SEQ ID Nos. 94, 104, and 114)

30 Determination of the whole base sequence of the cDNA
insert of clone HP02695 obtained from cDNA library of human
stomach cancer revealed the structure consisting of a 112-bp
5'-untranslated region, a 1020-bp ORF, and a 160-bp 3'-

untranslated region. The ORF codes for a protein consisting of 339 amino acid residues and there existed three putative transmembrane domains. Figure 34 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 38 kDa that was almost identical with the molecular weight of 38,274 kDa predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the rat hypertension-induced protein S-2 fragment (PIR Accession No. 539959). Table 23 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the rat hypertension-induced protein S-2 fragment (RN). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 74.3% in the entire region.

Determination of the whole base sequence of the cDNA insert of clone HP10031 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 55-bp 5'-untranslated region, a 1464-bp ORF, and a 649-bp 3'-untranslated region. The ORF codes for a protein consisting of 487 amino acid residues and there existed eleven putative transmembrane domains. Figure 35 depicts the hydrophobicity/hydrophilicity profile, obtained

by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight. When expressed in COS7 cells, an expression product of about 55 kDa was observed in the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein CELK07H8 (GenBank Accession No. AF047659). Table 24 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein CELK07H8 (CE). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 44.2% in the entire region.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for

example, Accession No. AA334000) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP10530> (SEQ ID Nos. 96, 106, and 116)

Determination of the whole base sequence of the cDNA insert of clone HP10530 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 80-bp 5'-untranslated region, a 1182-bp ORF, and a 95-bp 3'-untranslated region. The ORF codes for a protein consisting of 393 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 36 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 46 kDa that was somewhat larger than the molecular weight of 44,912 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 45.5 kDa from which the secretory signal is considered to have been cleaved. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from lysine at position 23. When expressed in COS7 cells, an expression product of about 43 kDa was observed in the supernatant fraction and the membrane fraction.

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The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the Arabidopsis thaliana hypothetical protein IG002N01 (GenBank Accession No. AF007269). Table 25 shows the comparison between amino acid sequences of the

30 Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA302913) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the

protein of the present invention.

<HP10541> (SEQ ID Nos. 97, 107, and 117)

Determination of the whole base sequence of the cDNA
5 insert of clone HP10541 obtained from cDNA library of human
stomach cancer revealed the structure consisting of a 7-bp
5'-untranslated region, a 591-bp ORF, and a 113-bp 3'-
untranslated region. The ORF codes for a protein consisting
of 196 amino acid residues and there existed a putative
10 secretory signal at the N-terminus. Figure 37 depicts the
hydrophobicity/hydrophilicity profile, obtained by the Kyte-
Doolittle method, of the present protein. In vitro
translation resulted in formation of a translation product
of 23 kDa that was somewhat larger than the molecular weight
15 of 21,553 predicted from the ORF. In this case, the addition
of a microsome led to the formation of a product of 20 kDa
from which the secretory signal is considered to have been
cleaved and a product of 23 kDa which is considered to have
a sugar chain being attached. Application of the (-3,-1)
20 rule, a method for predicting the cleavage site of the
secretory signal sequence, allows to expect that the mature
protein starts from glycine at position 41. In addition,
there exists in the amino acid sequence of this protein one
site at which N-glycosylation may occur (Asn-Leu-Thr at
25 position 185).

The search of the protein data base using the amino
acid sequence of the present protein revealed that the
protein was similar to the human zymogen membrane protein
(GenBank Accession No. AF056492). Table 26 shows the
30 comparison between amino acid sequences of the human protein
of the present invention (HP) and the human zymogen membrane
protein (ZM). Therein, the marks of -, *, and . represent a

gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 37.6% in the C-terminal region of 133 amino acid residues.

Table 26

10	HP MWRVPGTTRRPVTGESPGMHRPEAMLLLLTLALLGGPTWAGKMYGPGGGKYFS-TTEDYD	***.***** ** *
	ZM MLTVALLALLCASASGNAIQARSSSYSGEYGS GGGKRF SHSGNQLD	
	HP HEITGLRVS VGLLLVKS VQVKLGDSWDVKLGALGGNTQEVTLQPGEYITKV FVAFQAFLR	
	 * . * . . . * * *
	ZM GPITALRVRVNTYYIVGLQVRYGKVWSDYVGGRNGDLEEIFLHPGESVIQVSGKYKWLK	
15	HP GMVMYTSKDRYFYFGKLDGQISSAYPSQEGQVLVGIYQYQLLGKISIGFEWN-YPLEEP	
		. * . * . * . * . * . * . * . * . * . * . * . * . * . * . *
	ZM KLVFVTDKGRYLSFGKDSGTSFNAVPLHPNTVLRFISGRSGSL-IDAIGLHWDVYPTSCS	
	HP TTEPPVNLTYSANSPVGR	
20	ZM RC	

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA340605) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10550> (SEQ ID Nos. 98, 108, and 118)

Determination of the whole base sequence of the cDNA

Determination of the whole base sequence of the cDNA insert of clone HP10590 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 77-bp 5'-untranslated region, a 1053-bp ORF, and a 180-bp 3'-untranslated region. The ORF codes for a protein consisting of 350 amino acid residues and there existed one putative transmembrane domain. Figure 39 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 40 kDa that was almost identical with the molecular weight of 39,285 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of

43 kDa which is considered to have a sugar chain being attached. In addition, there exist in the amino acid sequence of this protein two sites at which N-glycosylation may occur (Asn-Asn-Ser at position 144 and Asn-Leu-Thr at position 328).

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA461346) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10591> (SEQ ID Nos. 100, 110, and 120)

Determination of the whole base sequence of the cDNA insert of clone HP10591 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 232-bp 5'-untranslated region, a 324-bp ORF, and a 844-bp 3'-untranslated region. The ORF codes for a protein consisting of 107 amino acid residues and there existed one putative transmembrane domain. Figure 40 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 11,328 predicted from the ORF.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H09424) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein

of the present invention.

<HP01462> (SEQ ID Nos. 121, 131, and 141)

Determination of the whole base sequence of the cDNA
5 insert of clone HP01462 obtained from cDNA library of human
fibrosarcoma cell line HT-1080 revealed the structure
consisting of a 121-bp 5'-untranslated region, a 1452-bp ORF,
and a 477-bp 3'-untranslated region. The ORF codes for a
protein consisting of 483 amino acid residues and there
10 existed a putative secretory signal at the N-terminus.
Figure 41 depicts the hydrophobicity/hydrophilicity profile,
obtained by the Kyte-Doolittle method, of the present
protein. In vitro translation resulted in formation of a
translation product of 72 kDa that was larger than the
15 molecular weight of 55,838 predicted from the ORF.
Application of the (-3,-1) rule, a method for predicting the
cleavage site of the secretory signal sequence, allows to
expect that the mature protein starts from lysine at
position 21.

20 The search of the protein data base using the amino
acid sequence of the present protein revealed that the
protein was similar to the *Caenorhabditis elegans*
hypothetical protein ZK1058.4 (EMBL Accession No. Z35604).
Table 27 shows the comparison between amino acid sequences
25 of the human protein of the present invention (HP) and the *C.*
elegans hypothetical protein ZK1058.4 (CE). Therein, the
marks of -, *, and . represent a gap, an amino acid residue
identical with that of the protein of the present invention,
and an amino acid residue similar to that of the protein of
30 the present invention, respectively. The both proteins
shared a homology of 35.6% in the entire region.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for

example, Accession No. AA307793) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP02485> (SEQ ID Nos. 122, 132, and 142)

Determination of the whole base sequence of the cDNA insert of clone HP02485 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 69-bp 5'-untranslated region, a 1005-bp ORF, and a 1672-bp 3'-untranslated region. The ORF codes for a protein consisting of 334 amino acid residues and there existed one putative transmembrane domain. Figure 42 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 36 kDa that was almost identical with the molecular weight of 38,171 predicted from the ORF. When expressed in COS7 cells, an expression product of about 23 kDa was observed in the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein W01A11.2 (GenBank Accession No. U64852). Table 28 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein W01A11.2 (CE). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 45.5% in the entire region.

Table 28

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HP                                MVEFAPLFMPWERRRLQTLAVLQFVFSFLALAEICT-V
5                                .***.***.***.***. ** .. *. . *
CE MRLRLSSISGKAKLPDKEICSSVSRI LAPLLVPWKRRLETLAVMGFIFMWVILPIMDLWV
HP GFIALLETRFWLLTVLYAAWYLD RDKPRQGGRIHQAIRCWTIWKYM KDYFPISLVKTAE
    * .*. **.*.***.* * *.***.***.***.***.
CE PFHVLENTTRWWFLVPLYAVWFYDFDTPKKASRRWNWARRHVAWKYFASYFPLRLIKTAD
10 HP LDPSRNYIAGFH PHGVLAVGAFANLCTESTGFSSIFPGIRPHLMMLTLWFRAPFFRDYIM
    * ..**** * ****.*.***.***.***.***.***.***.***.***.***.***.***.
CE LPADRNYIIGSHPHGMFSVGGFTAMSTNATGFEDKFP GIKSHIMTLNGQFYFPFRREFGI
HP SAGLVTSEKESA AHILNRKGGGNLLGIIVGGAQEALDARPGSF TLLLRNRKGFVRLALTH
    * .. *** ..... * *. .....***.***.*.***.***.***.***.***.
15 CE MLGGIEVSKE SLEYTLTKCGKGRACAIVIGGASEALEAHPNKNTLT LINRRGFCKYALKF
HP GAPLVPIFSFGENDLFDQIPNSSGSWLRYIQNRLQKIMGISLPLFHGRGVF-QYSFGLIP
    ** ***.....***.***.***.***.***.***.***.***.***.***.***.***.
CE GADLVPMYNFGENDLYEQYENPKGSRLREVQEKIKDMFGLCPPLLRGRSLFNQYLIGLLP
HP YRRPITTVVGKPIEVQKTLHPSEEEVNQLHQRYIKELCNLFEAHKLKFNIPADQHLEFC
20 .*.***.***.* *. *. *.***.***.***.***.***.***.***.***.***.***.
CE FRKPVTVMGRPIRVTQ TDEPTVEQIDELHAKYCDALYNLFEEYKHLHSIPPDTHLIFO

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25 Furthermore, the search of the GenBank using the base
sequences of the present cDNA has revealed the registration
of sequences that shared a homology of 90% or more (for
example, Accession No. D25664) in ESTs, but, since they are
partial sequences, it can not be judged whether or not any
of these sequences codes for the same protein as the protein
30 of the present invention.

<HP02798> (SEQ ID Nos. 123, 133, and 143)

Determination of the whole base sequence of the cDNA

Determination of the whole base sequence of the cDNA insert of clone HP10041 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 12-bp 5'-untranslated region, a 321-bp ORF, and a 286-bp 3'-untranslated region. The ORF codes for a protein consisting of 106 amino acid residues and there existed one putative transmembrane domain. Figure 44 depicts

the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 12,060 predicted from the ORF. When expressed in COS7 cells, an expression product of about 13 kDa was observed in the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein K10B2.4 (GenBank Accession No. U28730). Table 30 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein K10B2.4 (CE). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 62.1% in the entire region.

Table 30

HP	MSTNNMSDPRRPKNKVLRYKP---PPSECNPALDDPTPDYMNLLGMIFSMCGLMUKLKWCA
	.****.*.....** *.....*
CE	MQQNGDPRRTNRIVRYKPLDSTANQQQAISEDPLPEYMNVLGMIFSMCGLMIRKWC
HP	WVAVYCSFISFANSRSEDTKQMMSSFMLSISAVVMSYLQNPQPMTPPW
	.. ** *****.*.*.*.....***** *.....*
CE	WLALVCSCISFANTRTSDDAKQIVSSFMLSISAVVMSYLQNPSPPIPPWVTLQ

Furthermore, the search of the GenBank using the base

sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H20098) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10246> (SEQ ID Nos. 125, 135, and 145)

Determination of the whole base sequence of the cDNA insert of clone HP10246 obtained from cDNA library of human epidermoid carcinoma cell line KB revealed the structure consisting of a 110-bp 5'-untranslated region, a 675-bp ORF, and a 79-bp 3'-untranslated region. The ORF codes for a protein consisting of 224 amino acid residues and there existed five putative transmembrane domains. Figure 45 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 23 kDa that was somewhat smaller than the molecular weight of 25,244 predicted from the ORF. When expressed in COS7 cells, an expression product of about 21 kDa was observed in the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human putative seven transmembrane domain protein (GenBank Accession No. Y18007). Table 31 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human putative seven transmembrane domain protein (TM). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that

of the protein of the present invention, respectively. The both proteins shared a homology of 93.3% in the entire region.

5

Table 31

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15

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HP MTLFHFGNCFALAYFPYFITYKCSGLSEYNAFWKCVQAGVTYLFVQLCKMLFLATFFPTW
*****.*****
TM MTLFHFGNCFALAYFPYFITYKCTDLSEYNAFWKCVQAGVTYLFVQLCKMLFLATFFPTW
HP EGGIYDFIGEFMKASVDVADLIGLNLVMSRNAGKGEYKIMVAALGWATAELIMSRCIPLW
*****
TM EGGIYDFIGEFMKASVDVADLIGLNLVMSRNAGKGEYKIMVAALGWATAELIMSRCIPLW
HP VGARGIEFDWKYIQMSIDSNISLVHYIVASAQVWMITRYDLYHTFRPAVLLLMFLSVYKA
*****.*****
TM VGARGIEFDWKYIQMSIDSNISLGPYIVASAQVWMITRYDLYHTFRPAVLLLMFLRVYKA
HP FVMETFVHLCSLGSWAALLARAVVTGLLALSTLALYVAVVNVHS
*****.*.*.***.***.....*.*****
TM FVMETFVHLCSLGSWAVLMAGVVVKGLLVIRNLAMYVAVVNVHS

```

20

25

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA453931) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

30

<HP10392> (SEQ ID Nos. 126, 136, and 146)

Determination of the whole base sequence of the cDNA insert of clone HP10392 obtained from cDNA library of human osteosarcoma cell line U-2 OS revealed the structure

consisting of a 24-bp 5'-untranslated region, a 777-bp ORF, and a 726-bp 3'-untranslated region. The ORF codes for a protein consisting of 258 amino acid residues and there existed a putative secretory signal at the N-terminus.

5 Figure 46 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 34 kDa that was somewhat larger than the molecular weight of 29,623 predicted from the ORF.
10 Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from leucine at position 49.

Furthermore, the search of the GenBank using the base
15 sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H15999) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein
20 of the present invention. In addition, partial identity with the hypothetical protein KIAA0384 (Accession No. AB002382) was observed, although the hypothetical protein had a different ORF.

25 <HP10489> (SEQ ID Nos. 127, 137, and 147)

Determination of the whole base sequence of the cDNA insert of clone HP10489 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 137-bp 5'-untranslated region, a 333-bp ORF, and a 189-bp 3'-
30 untranslated region. The ORF codes for a protein consisting of 110 amino acid residues and there existed two putative transmembrane domains. Figure 47 depicts the

hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 19 kDa that was somewhat larger than the molecular weight of 12,010 predicted from the ORF.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA262162) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10519> (SEQ ID Nos. 128, 138, and 148)

Determination of the whole base sequence of the cDNA insert of clone HP10519 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 67-bp 5'-untranslated region, a 276-bp ORF, and a 367-bp 3'-untranslated region. The ORF codes for a protein consisting of 91 amino acid residues and there existed one putative transmembrane domain. Figure 48 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 10 kDa that was almost identical with the molecular weight of 10,275 predicted from the ORF.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. W16639) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein

by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from serine at position 36.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Drosophila melanogaster* GOLIATH protein (SWISS-PROT Accession No. Q06003). Table 32 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *D. melanogaster* GOLIATH protein (DM). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The intermediate region of 169 amino acids of the protein of the present invention shared a homology of 41.4% with the N-terminal region of the *D. melanogaster* GOLIATH protein.

The present invention provides human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as eucaryotic cells expressing these DNAs. All of the proteins of the present invention are secreted or exist in the cell membrane, so that they are considered to be proteins controlling the proliferation and/or the differentiation of the cells. Accordingly, the proteins of the present invention can be employed as pharmaceuticals such as carcinostatic agents which act to control the proliferation and/or the differentiation of the cells, or as antigens for preparing antibodies against these proteins. The DNAs of the present invention can be utilized as probes for the genetic diagnosis and gene sources for the gene therapy. Furthermore, the DNAs can be utilized for large-scale expression of these proteins. Cells into which these genes are introduced to express these proteins, can be utilized for detection of the corresponding receptors and ligands, screening of novel low-molecular pharmaceuticals, and so on.

The present invention also provides genes corresponding to the polynucleotide sequences disclosed herein. "Corresponding genes" are the regions of the genome that are transcribed to produce the mRNAs from which cDNA polynucleotide sequences are derived and may include contiguous regions of the genome necessary for the regulated expression of such genes. Corresponding genes may therefore include but are not limited to coding sequences, 5' and 3' untranslated regions, alternatively spliced exons, introns, promoters, enhancers, and silencer or suppressor elements. The corresponding genes can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include the preparation of probes or

primers from the disclosed sequence information for identification and/or amplification of genes in appropriate genomic libraries or other sources of genomic materials. An "isolated gene" is a gene that has been separated from the adjacent coding sequences, if any, present in the genome of the organism from which the gene was isolated.

Organisms that have enhanced, reduced, or modified expression of the gene(s) corresponding to the polynucleotide sequences disclosed herein are provided. The desired change in gene expression can be achieved through the use of antisense polynucleotides or ribozymes that bind and/or cleave the mRNA transcribed from the gene (Albert and Morris, 1994, Trends Pharmacol. Sci. 15(7): 250-254; Lavarosky et al., 1997, Biochem. Mol. Med. 62(1): 11-22; and Hampel, 1998, Prog. Nucleic Acid Res. Mol. Biol. 58: 1-39; all of which are incorporated by reference herein). Transgenic animals that have multiple copies of the gene(s) corresponding to the polynucleotide sequences disclosed herein, preferably produced by transformation of cells with genetic constructs that are stably maintained within the transformed cells and their progeny, are provided. Transgenic animals that have modified genetic control regions that increase or reduce gene expression levels, or that change temporal or spatial patterns of gene expression, are also provided (see European Patent No. 0 649 464 B1, incorporated by reference herein). In addition, organisms are provided in which the gene(s) corresponding to the polynucleotide sequences disclosed herein have been partially or completely inactivated, through insertion of extraneous sequences into the corresponding gene(s) or through deletion of all or part of the corresponding gene(s). Partial or complete gene inactivation can be accomplished

through insertion, preferably followed by imprecise excision, of transposable elements (Plasterk, 1992, Bioessays 14(9): 629-633; Zwaal et al., 1993, Proc. Natl. Acad. Sci. USA 90(16): 7431-7435; Clark et al., 1994, Proc. Natl. Acad. Sci. USA 91(2): 719-722; all of which are incorporated by reference herein), or through homologous recombination, preferably detected by positive/negative genetic selection strategies (Mansour et al., 1988, Nature 336: 348-352; U.S. Patent Nos. 5,464,764; 5,487,992; 5,627,059; 5,631,153; 5,614, 396; 5,616,491; and 5,679,523; all of which are incorporated by reference herein). These organisms with altered gene expression are preferably eukaryotes and more preferably are mammals. Such organisms are useful for the development of non-human models for the study of disorders involving the corresponding gene(s), and for the development of assay systems for the identification of molecules that interact with the protein product(s) of the corresponding gene(s). Where the protein of the present invention is membrane-bound (e.g., is a receptor), the present invention also provides for soluble forms of such protein. In such forms part or all of the intracellular and transmembrane domains of the protein are deleted such that the protein is fully secreted from the cell in which it is expressed. The intracellular and transmembrane domains of proteins of the invention can be identified in accordance with known techniques for determination of such domains from sequence information.

Proteins and protein fragments of the present invention include proteins with amino acid sequence lengths that are at least 25% (more preferably at least 50%, and most preferably at least 75%) of the length of a disclosed protein and have at least 60% sequence identity (more

50 base pairs in length should be 5-10°C less than the melting temperature (T_m) of the hybrid, where T_m is determined according to the following equations. For hybrids less than 18 base pairs in length, $T_m(^{\circ}\text{C}) = 2(\text{\# of A + T bases}) + 4(\text{\# of G + C bases})$. For hybrids between 18 and 49 base pairs in length, $T_m(^{\circ}\text{C}) = 81.5 + 16.6(\log_{10}[\text{Na}^+]) + 0.41(\% \text{G+C}) - (600/N)$, where N is the number of bases in the hybrid, and $[\text{Na}^+]$ is the concentration of sodium ions in the hybridization buffer ($[\text{Na}^+]$ for 1×SSC=0.165M).

Additional examples of stringency conditions for polynucleotide hybridization are provided in Sambrook, J., E.F. Fritsch, and T. Maniatis, 1989, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, chapters 9 and 11, and *Current Protocols in Molecular Biology*, 1995, F.M. Ausubel et al., eds., John Wiley & Sons, Inc., sections 2.10 and 6.3-6.4, incorporated herein by reference.

Preferably, each such hybridizing polynucleotide has a length that is at least 25% (more preferably at least 50%, and most preferably at least 75%) of the length of the polynucleotide of the present invention to which it hybridizes, and has at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% or 95% identity) with the polynucleotide of the present invention to which it hybridizes, where sequence identity is determined by comparing the sequences of the hybridizing polynucleotides when aligned so as to maximize overlap and identity while minimizing sequence gaps.

CLAIMS

1. A protein comprising any one of an amino acid sequence selected from the group consisting of SEQ ID Nos. 1 to 10, 31 to 40, 61 to 70, 91 to 100, and 121 to 130.
5
2. An isolated DNA coding for the protein according to Claim 1.
3. An isolated cDNA comprising any one of a base sequence selected from the group consisting of SEQ ID Nos. 11 to 20, 41 to 50, 71 to 80, 101 to 110, and 131 to 140.
10
4. The cDNA according to Claim 3 consisting of any one of a base sequence selected from the group consisting of SEQ ID Nos. 21 to 30, 51 to 60, 81 to 90, 111 to 120, and 141 to 150.
- 15 5. An expression vector that is capable of expressing the DNA according to any one of Claim 2 to Claim 4 by in vitro translation or in eucaryotic cells.
6. A transformed eucaryotic cell that is capable of expressing the DNA according to any one of Claim 2 to Claim 4 and of producing the protein according to Claim 1.
20

PCT

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10/208820 24 July 1998 (24.07.98) JP 10/224105 7 August 1998 (07.08.98) JP 10/238116 25 August 1998 (25.08.98) JP 10/254736 9 September 1998 (09.09.98) JP 10/275505 29 September 1998 (29.09.98) JP			
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(75) Inventors/Applicants (for US only): KATO, Seishi [JP/JP]; 3-46-50, Wakamatsu, Sagamihara-shi, Kanagawa 229-0014 (JP). KIMURA, Tomoko [JP/JP]; 302, 4-1-28, Nishiikuta, Tama-ku, Kawasaki-shi, Kanagawa 214-0037 (JP).		With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.	
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(57) Abstract			
The present invention provides human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as eucaryotic cells expressing these DNAs.			

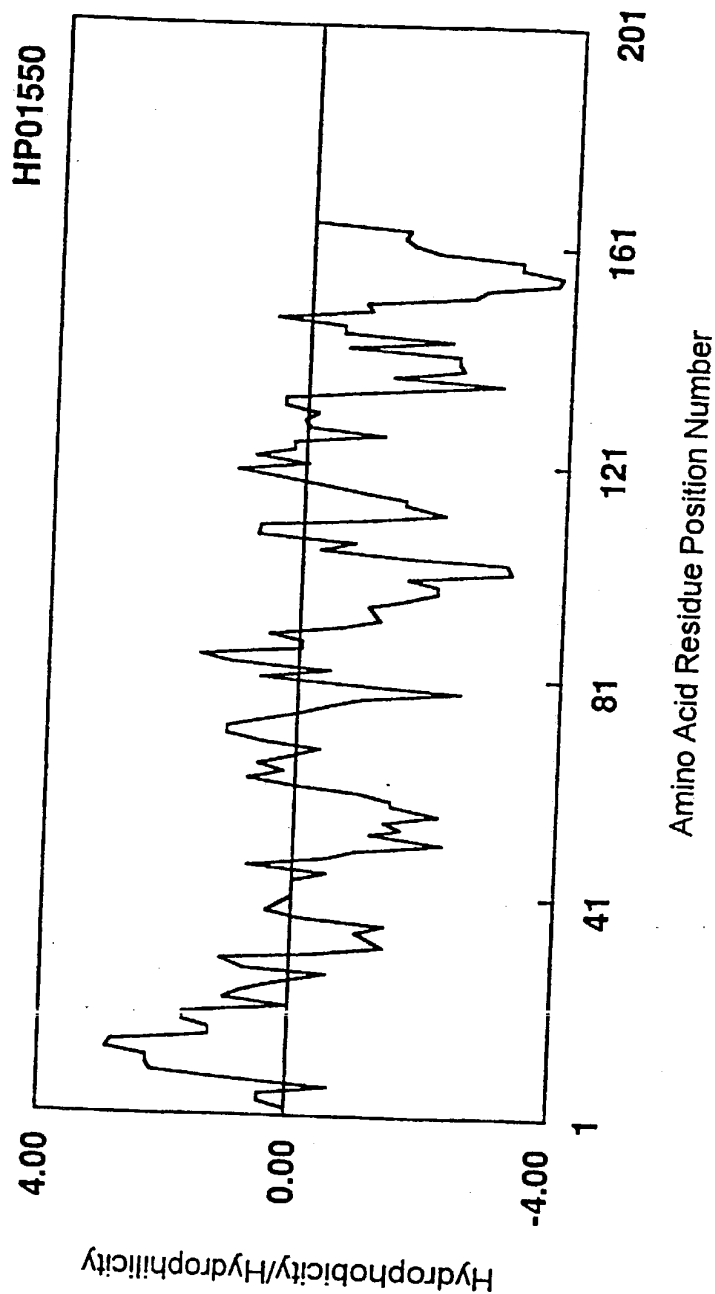


Fig. 1

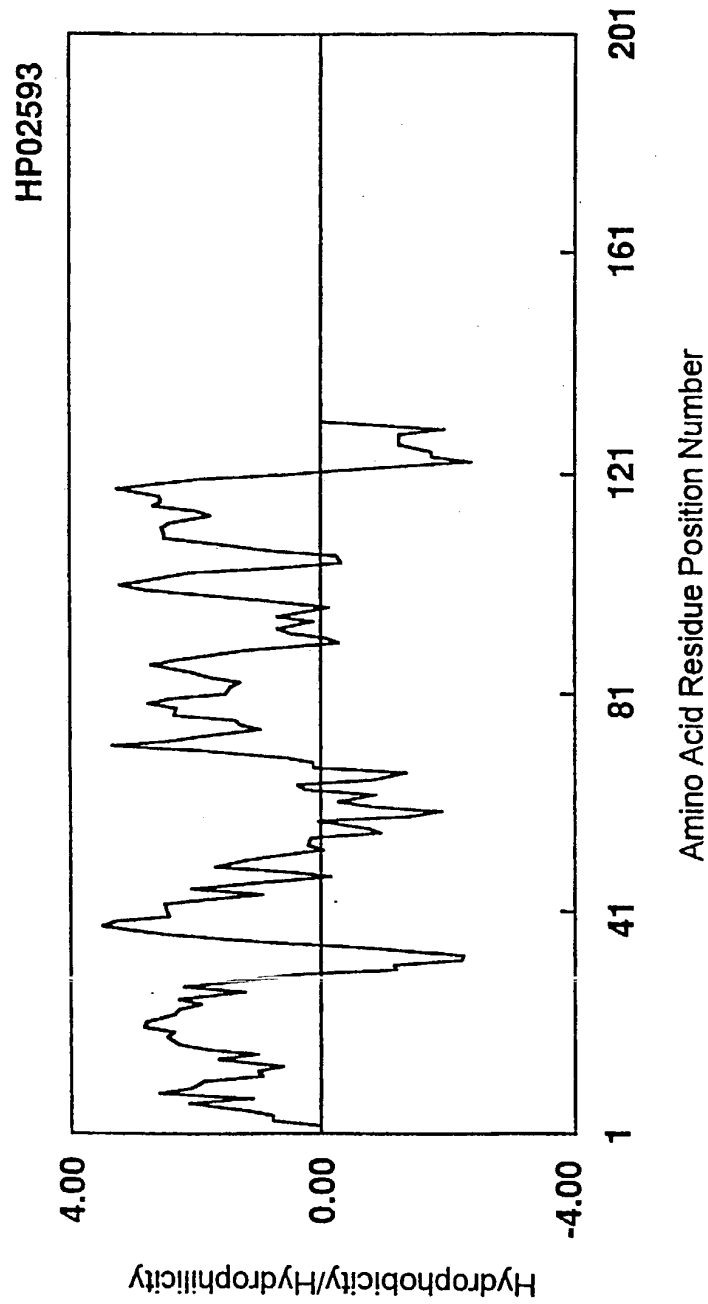


Fig. 2

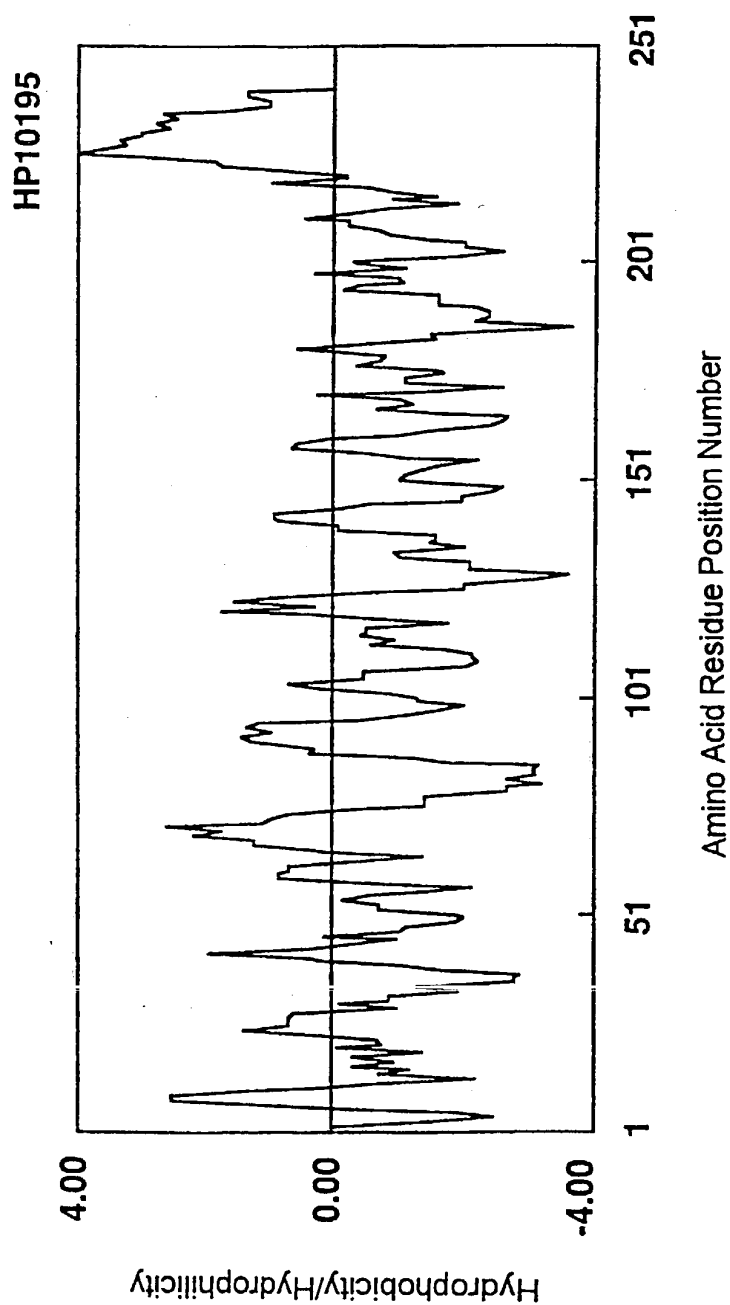


Fig. 3

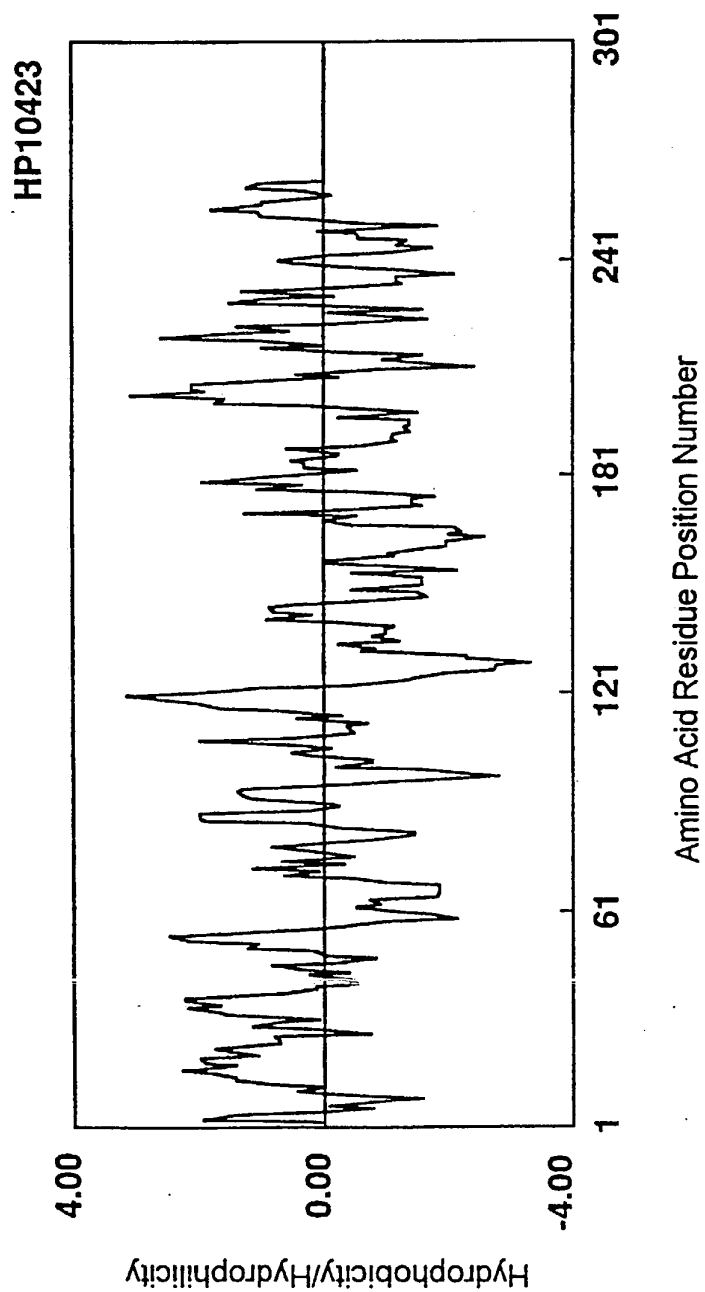


Fig. 4

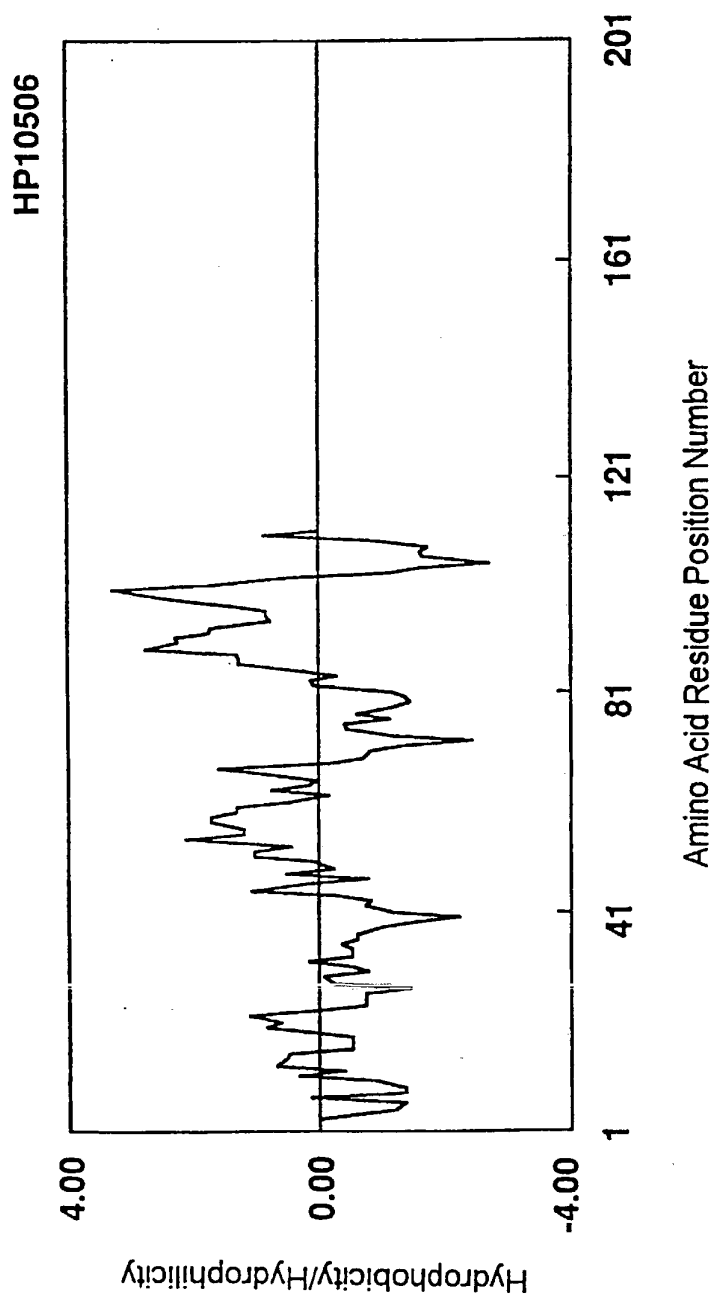


Fig. 5

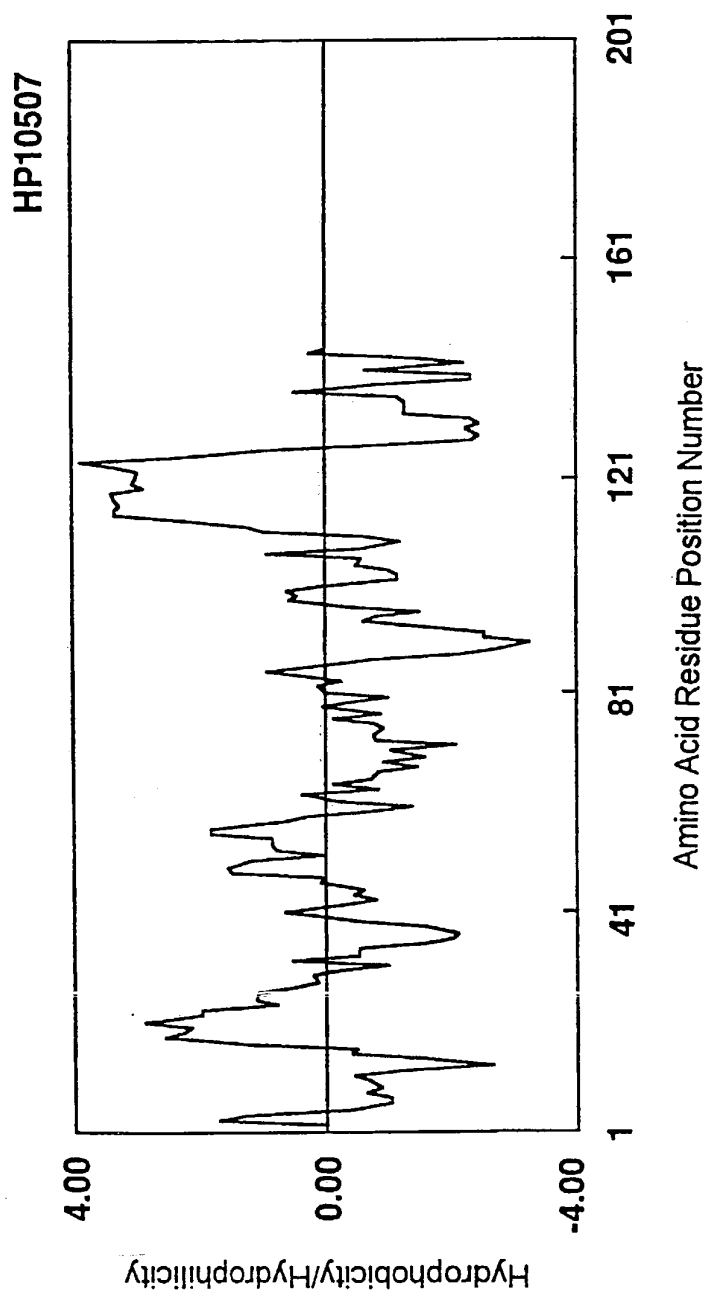


Fig. 6

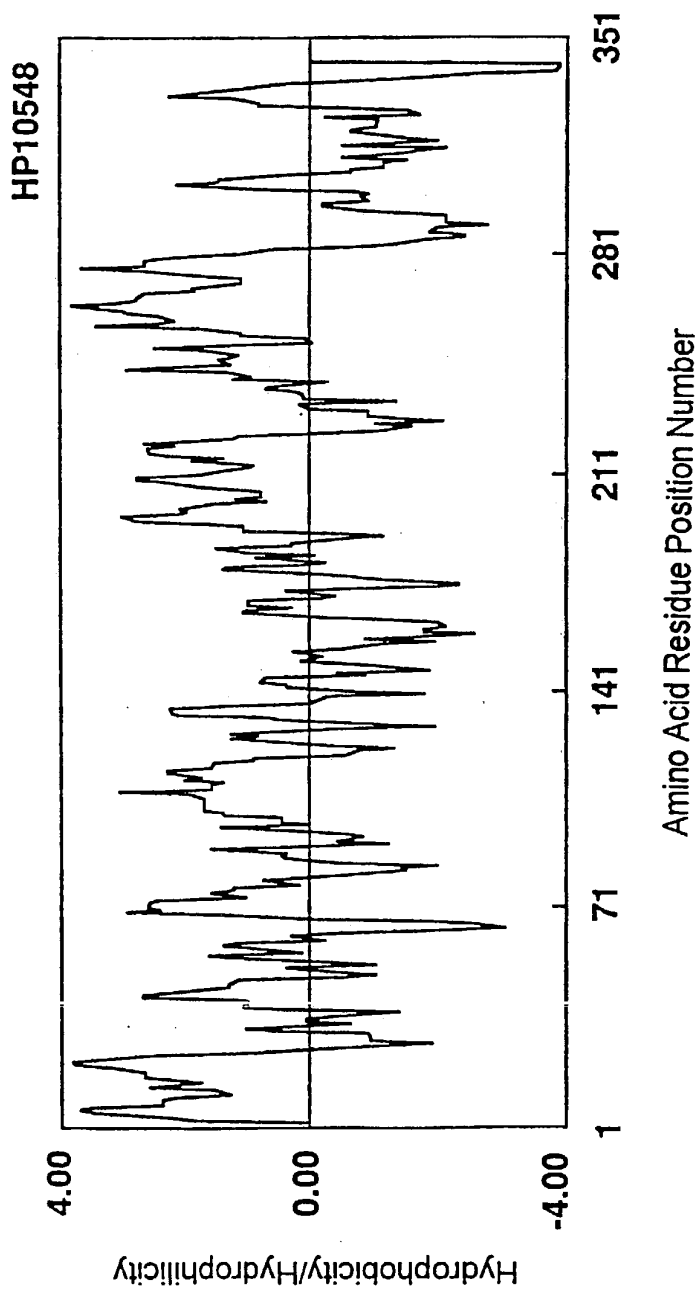


Fig. 7

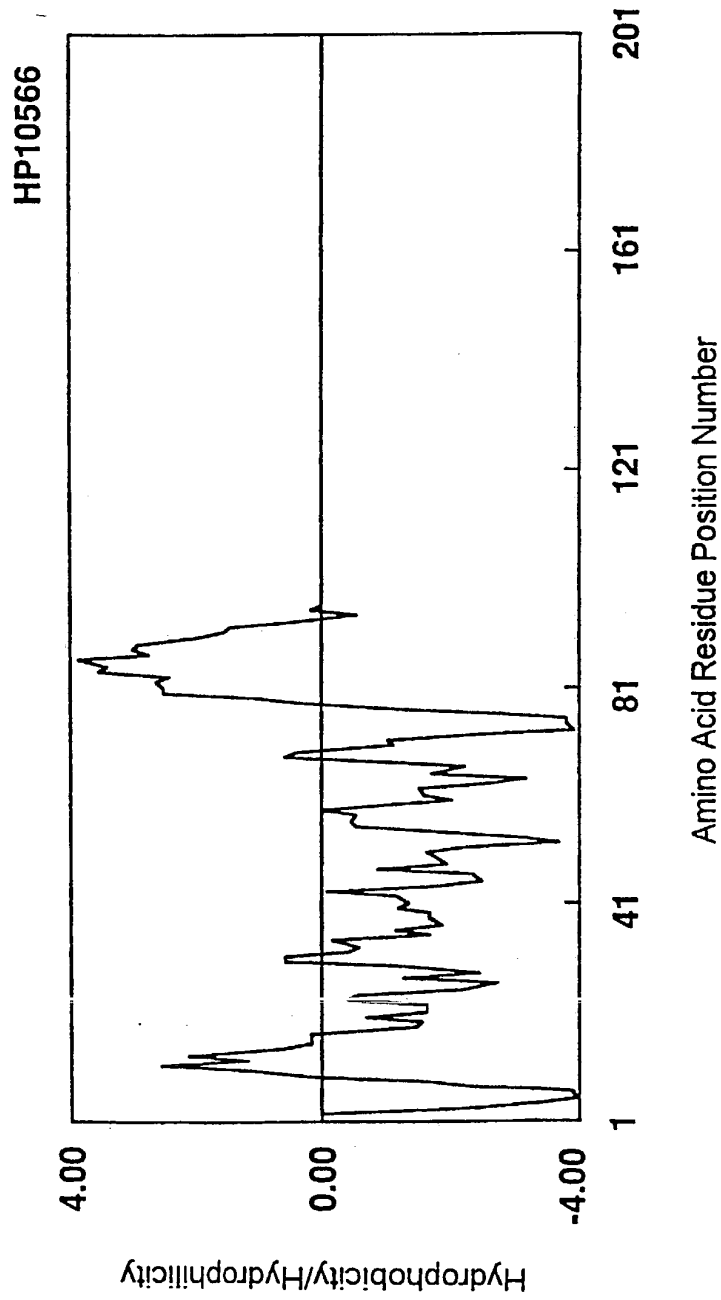


Fig. 8

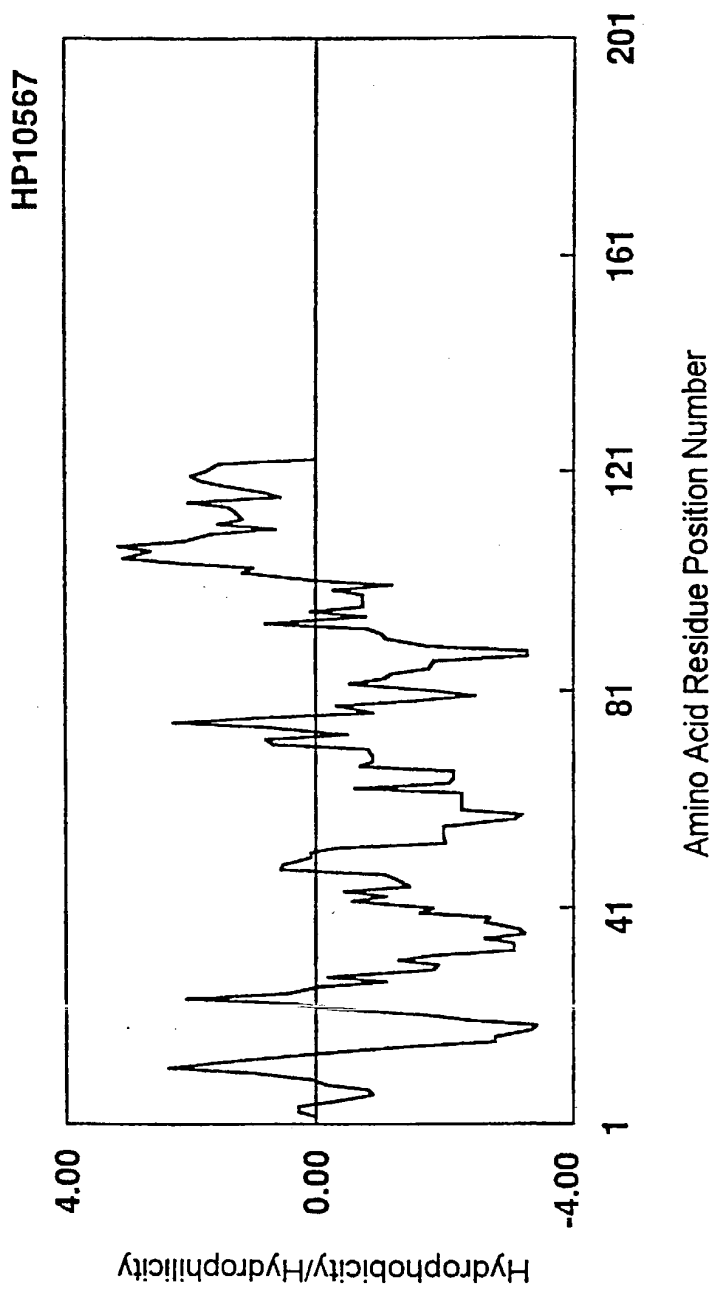


Fig. 9

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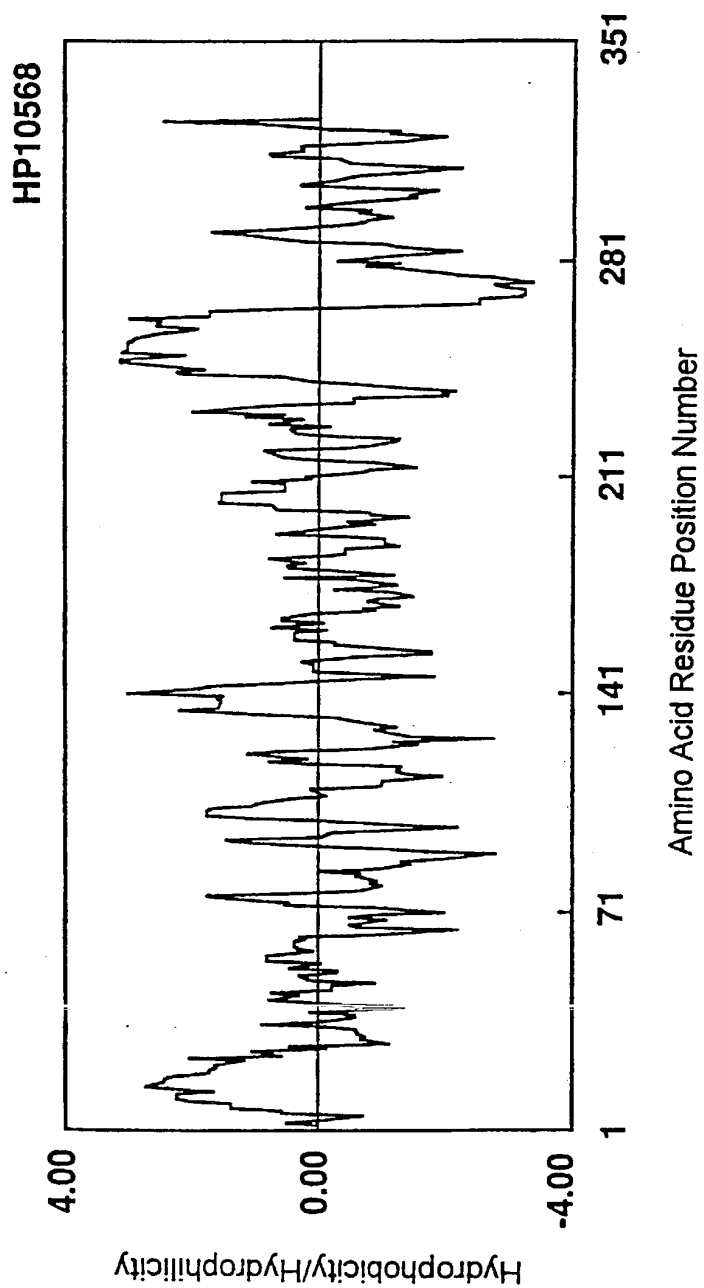


Fig. 10

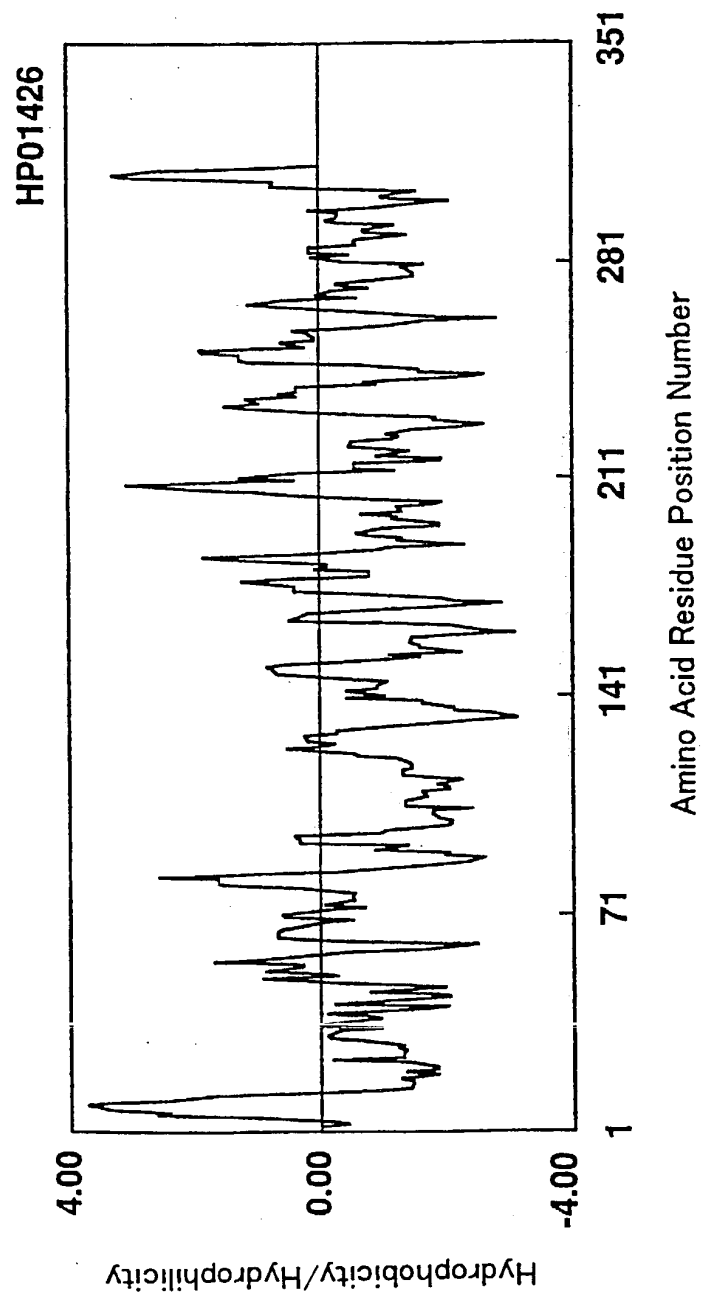


Fig. 11

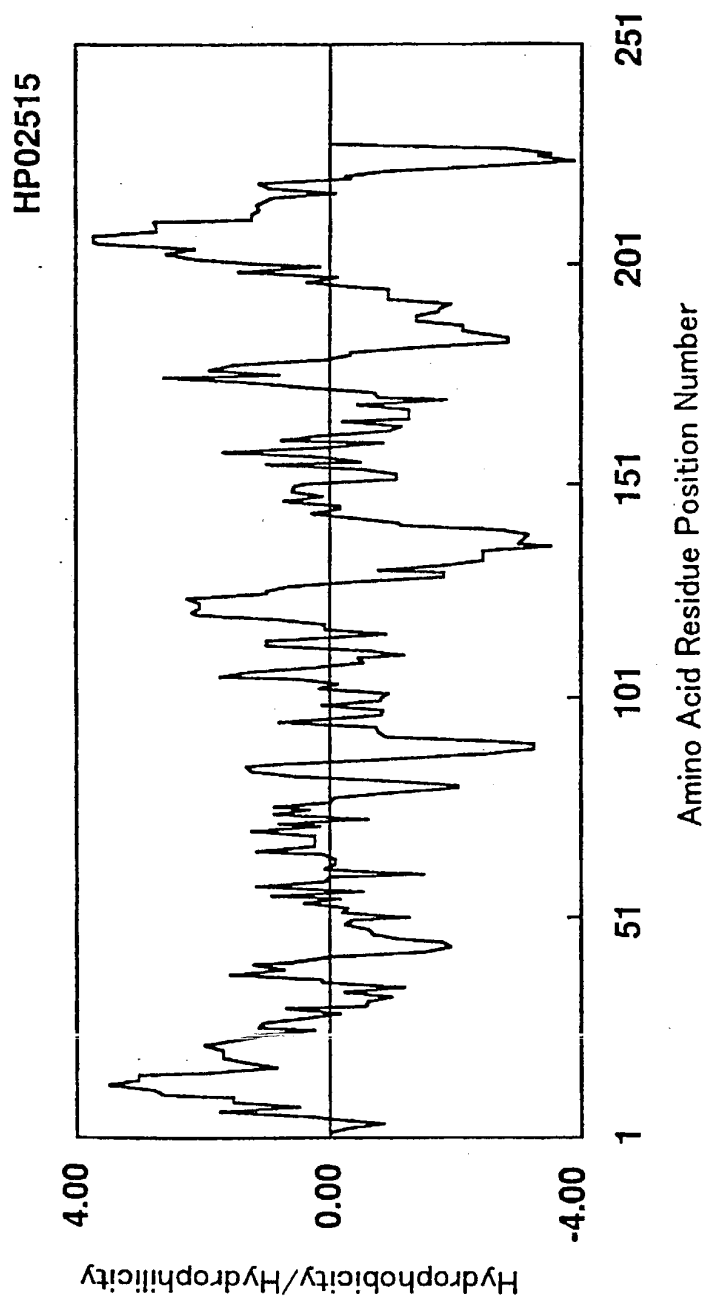


Fig.12

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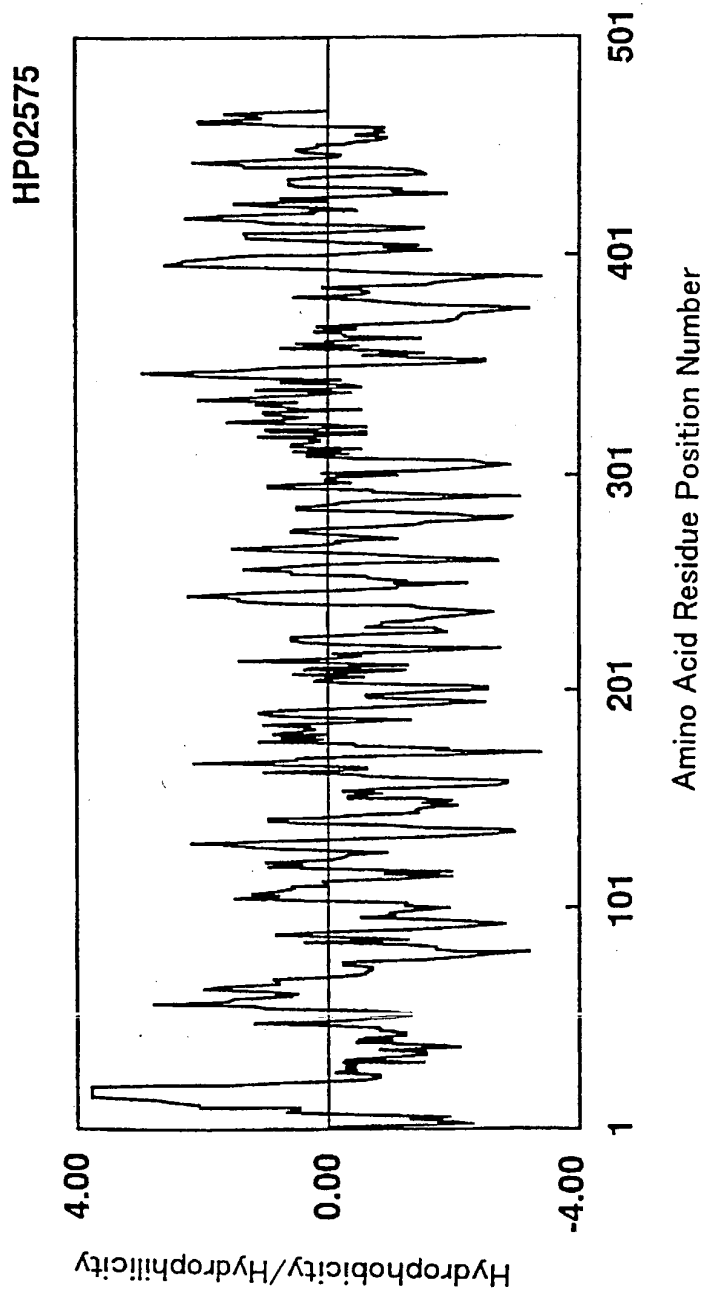


Fig. 13

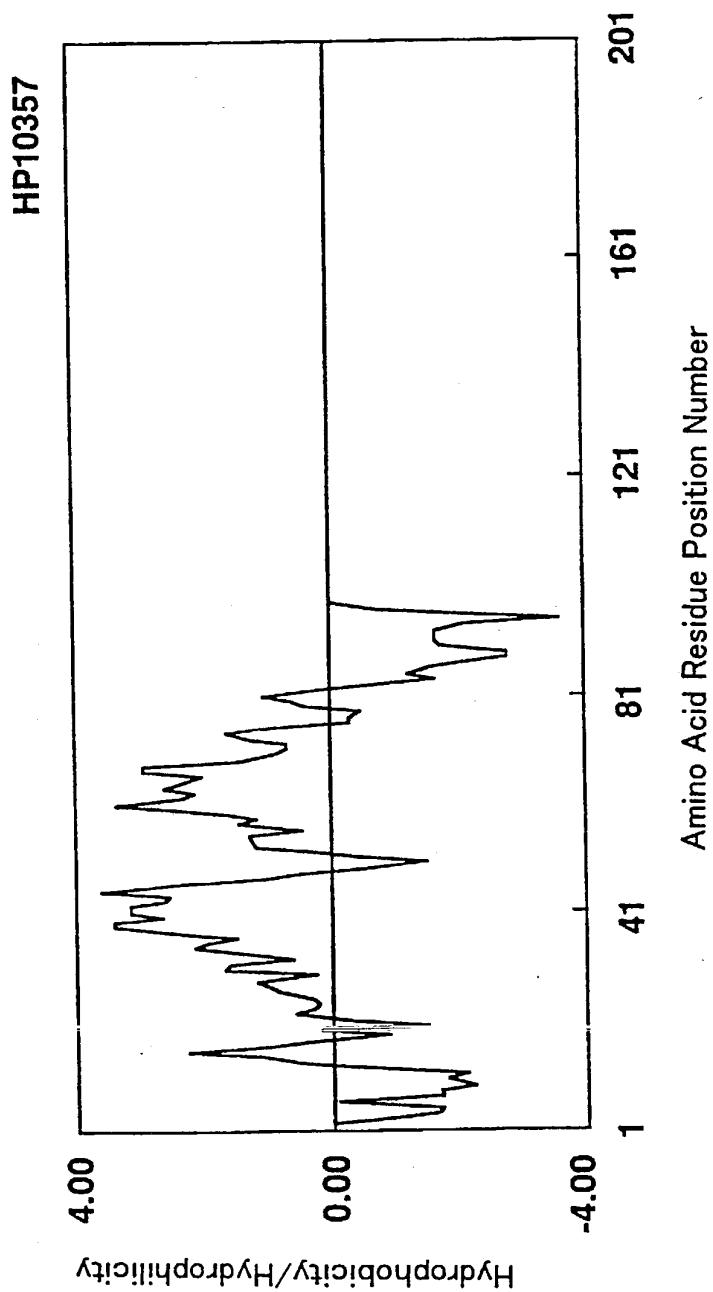


Fig. 14

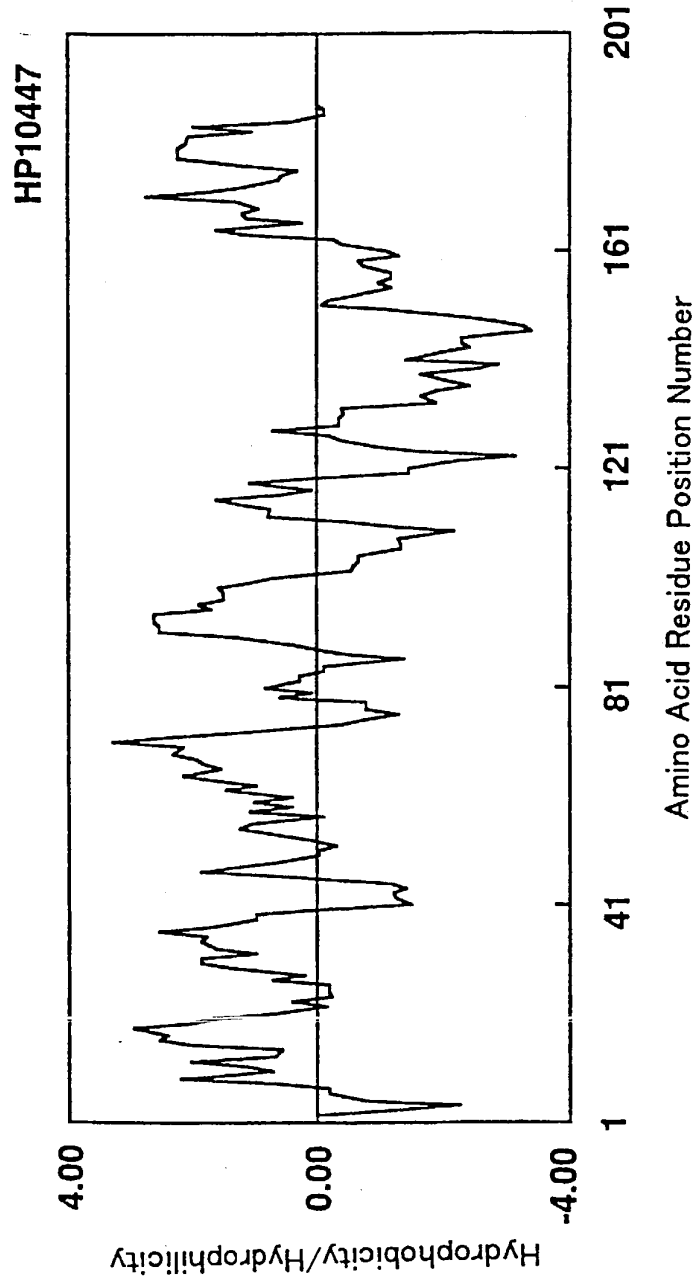


Fig. 15

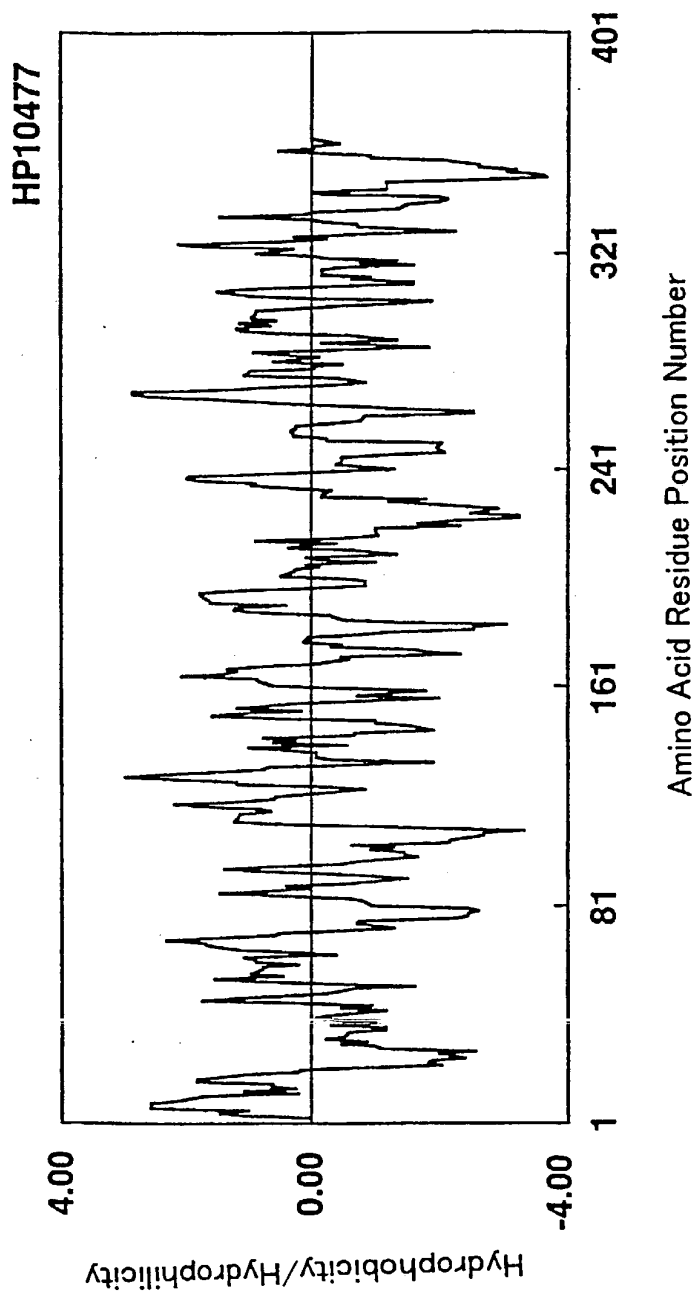


Fig. 16

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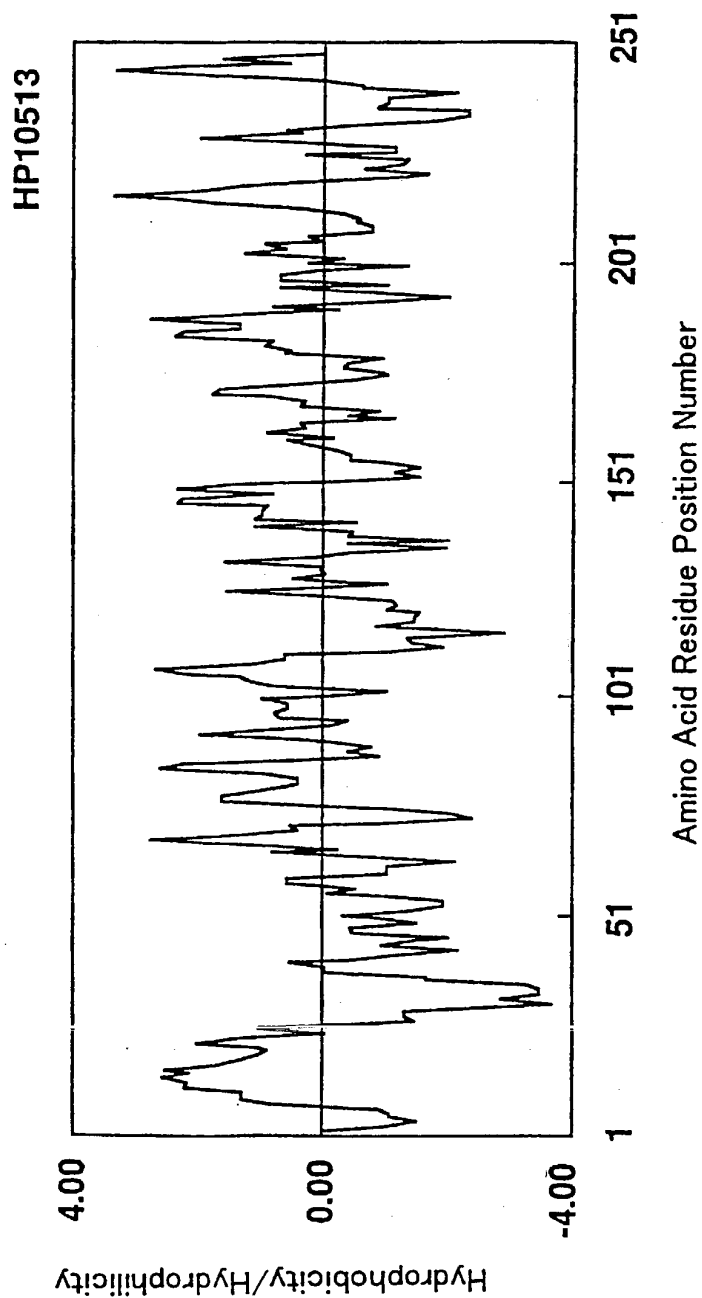


Fig.17

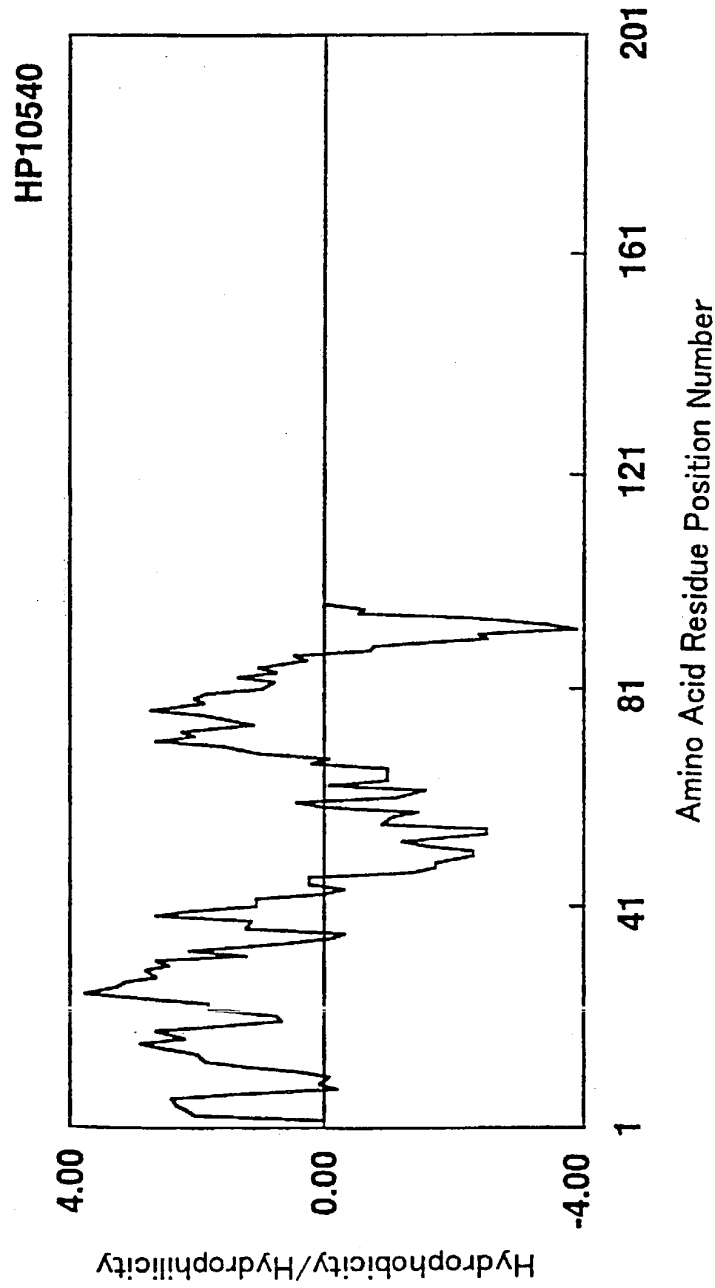


Fig. 18

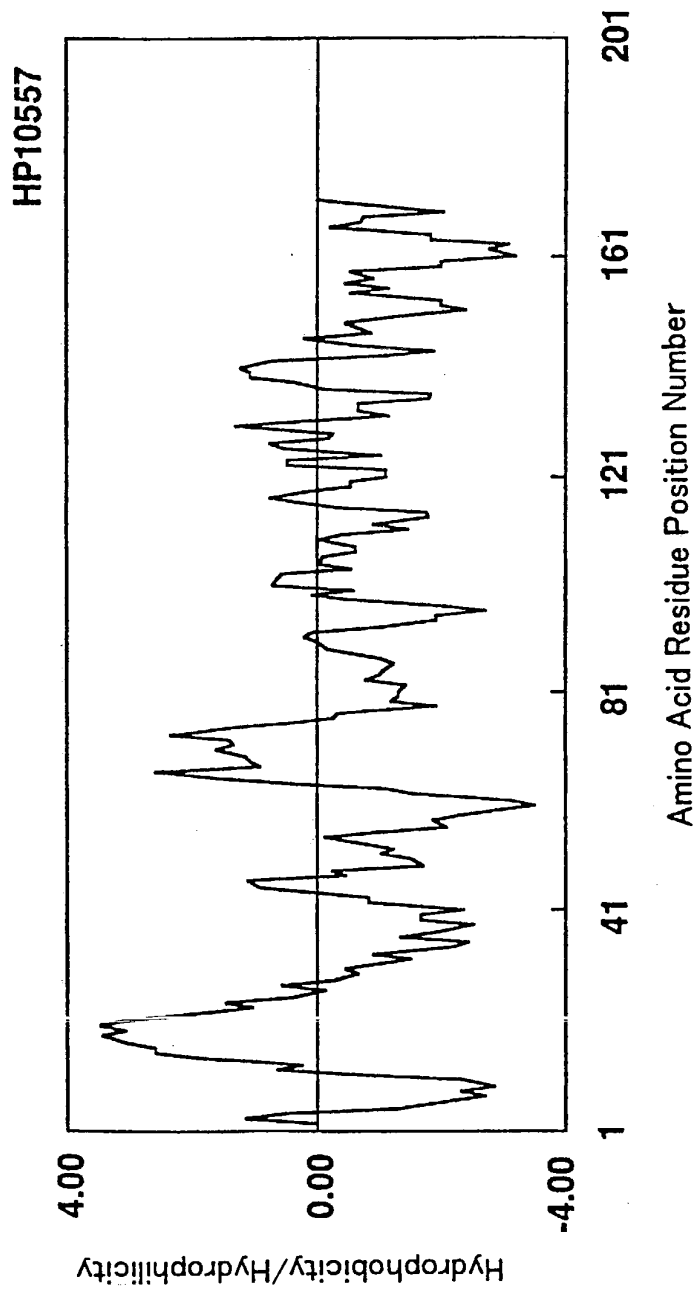


Fig. 19

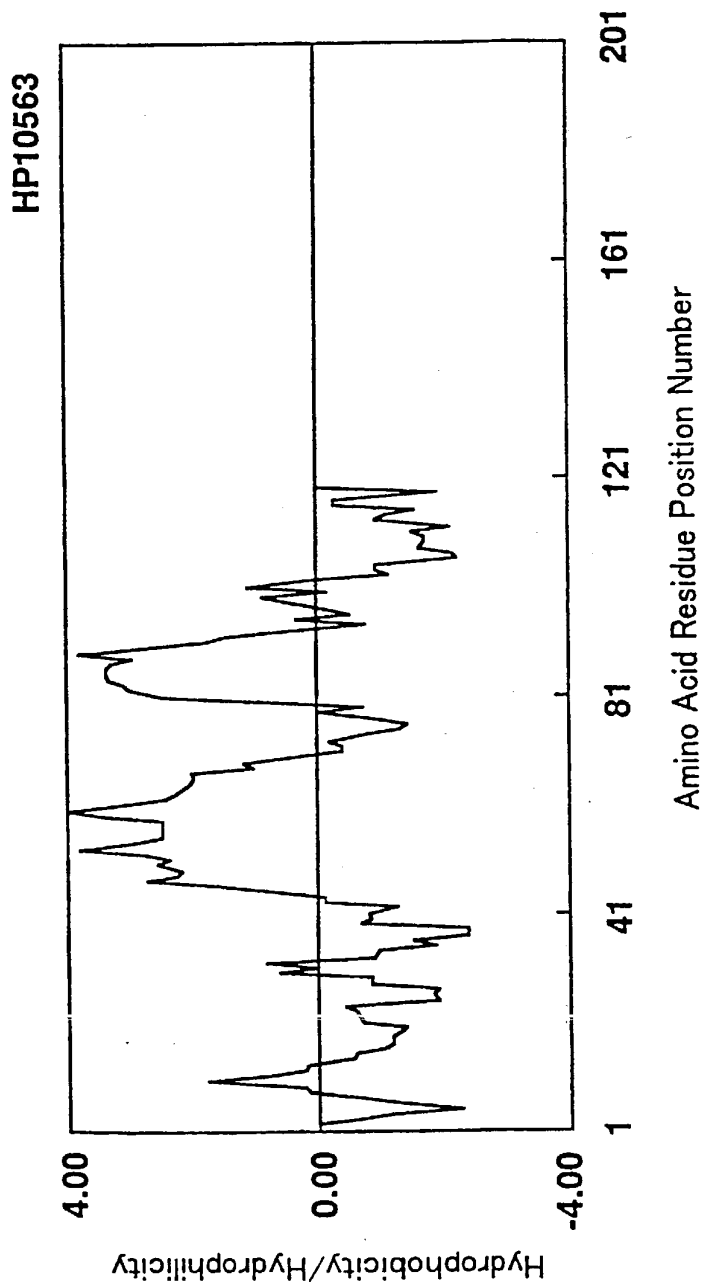


Fig. 20

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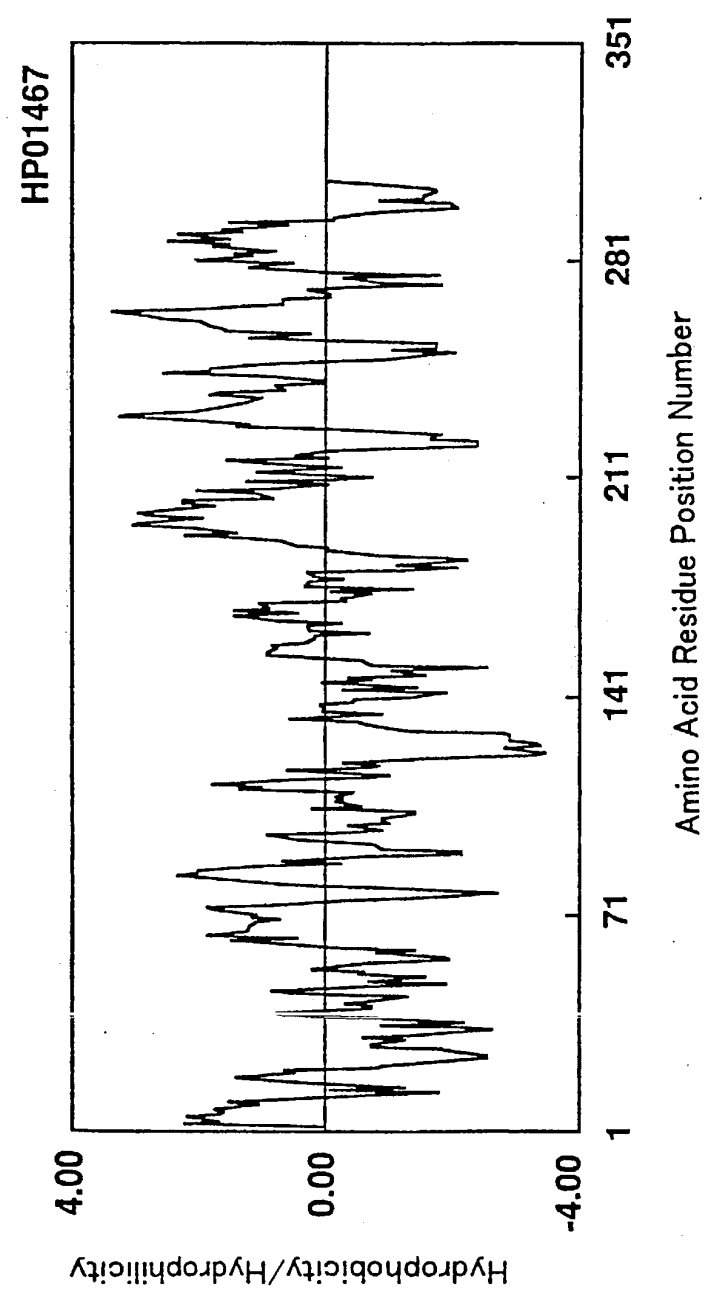


Fig. 21

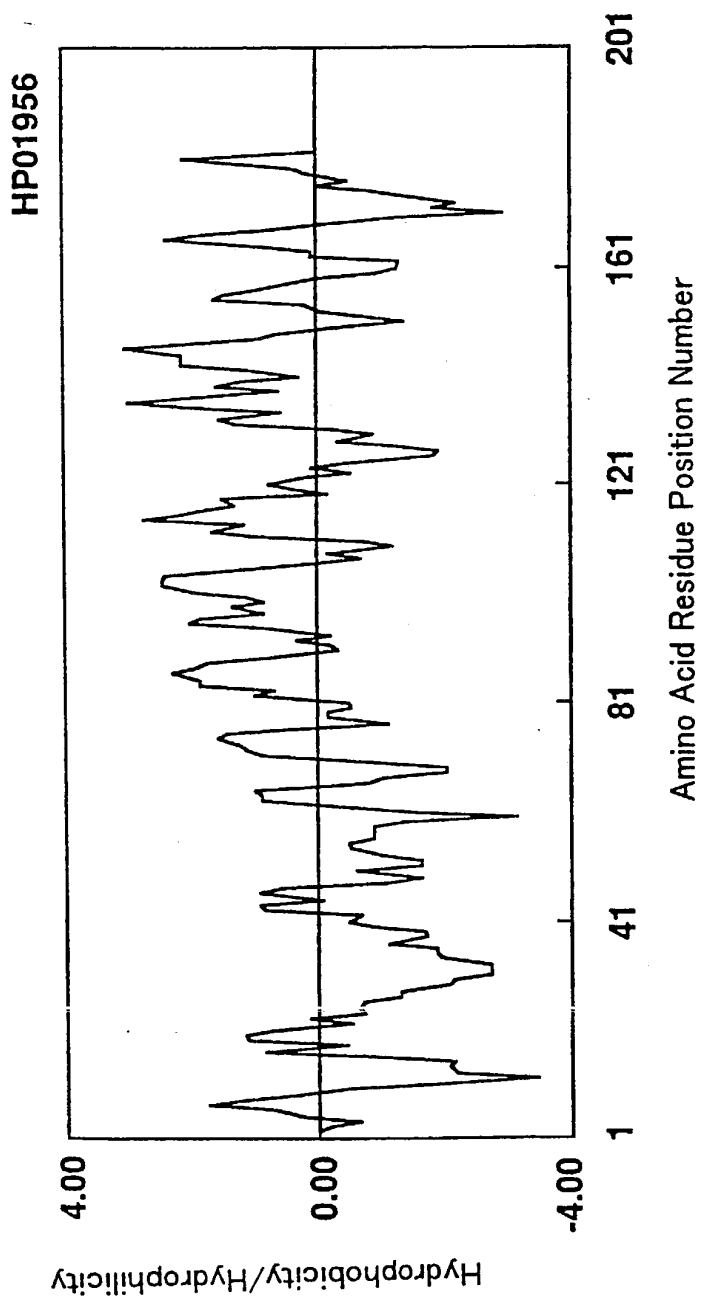


Fig.22

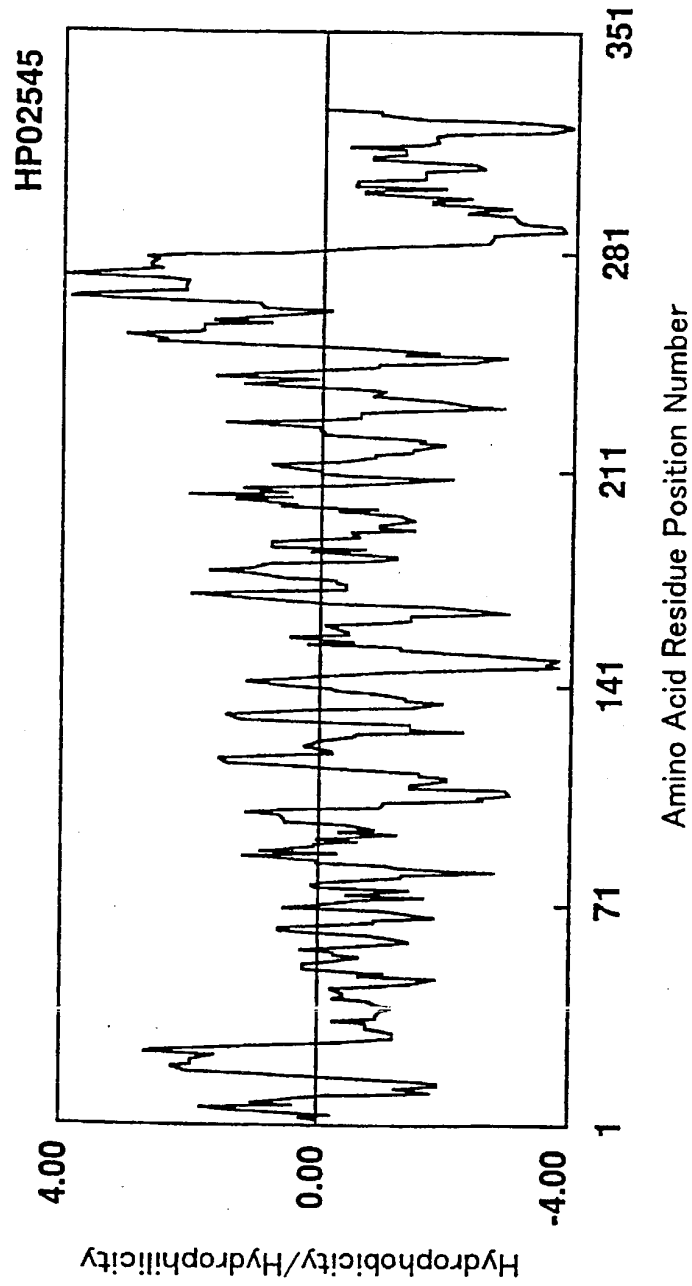


Fig. 23

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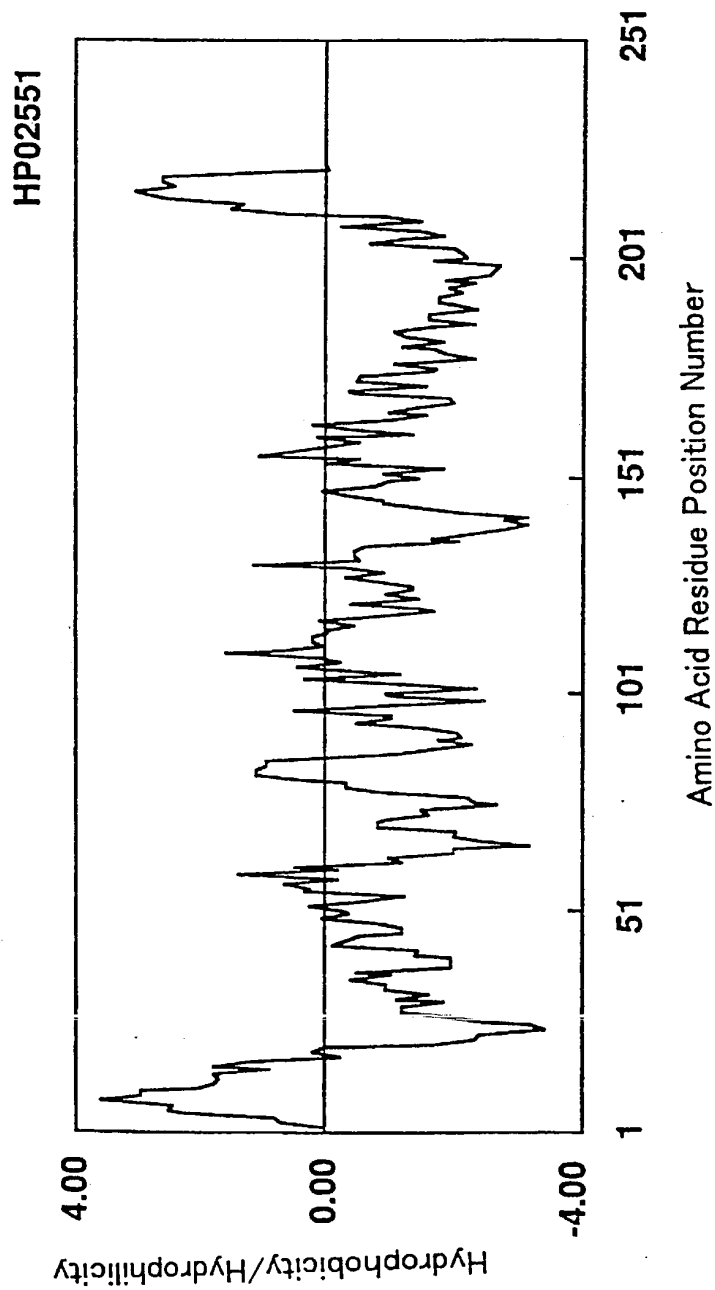


Fig. 24

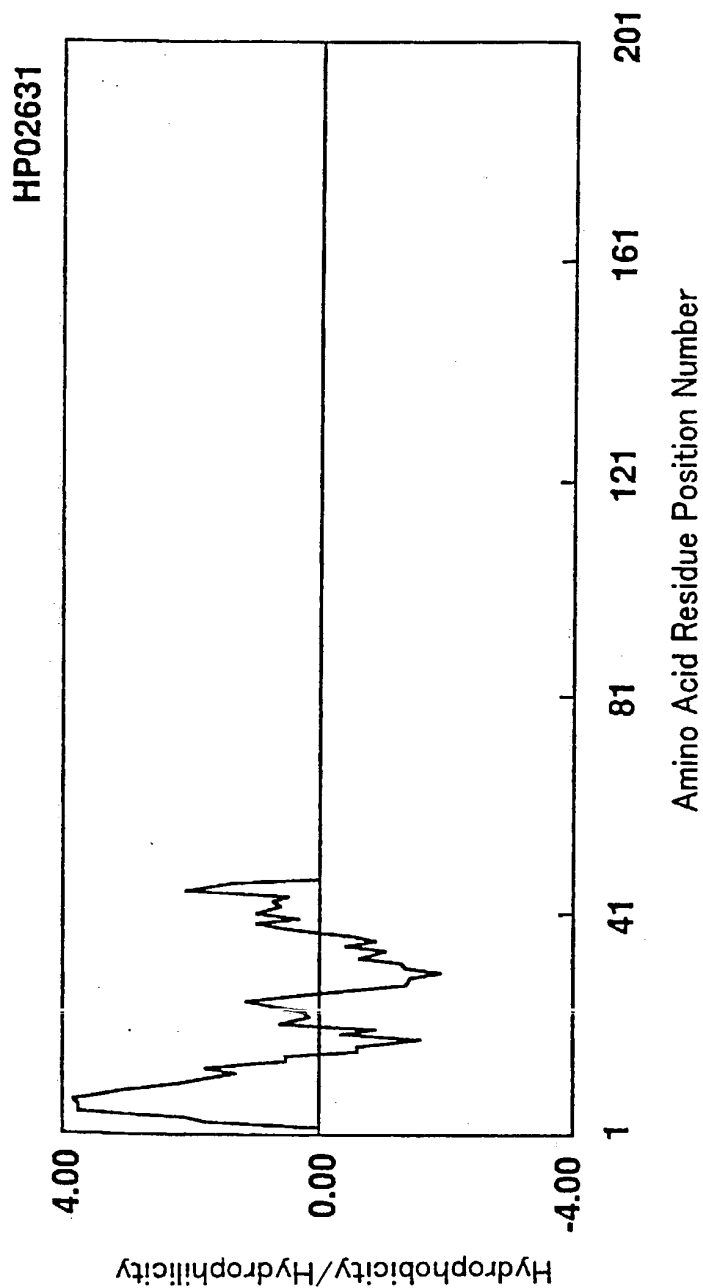


Fig. 25

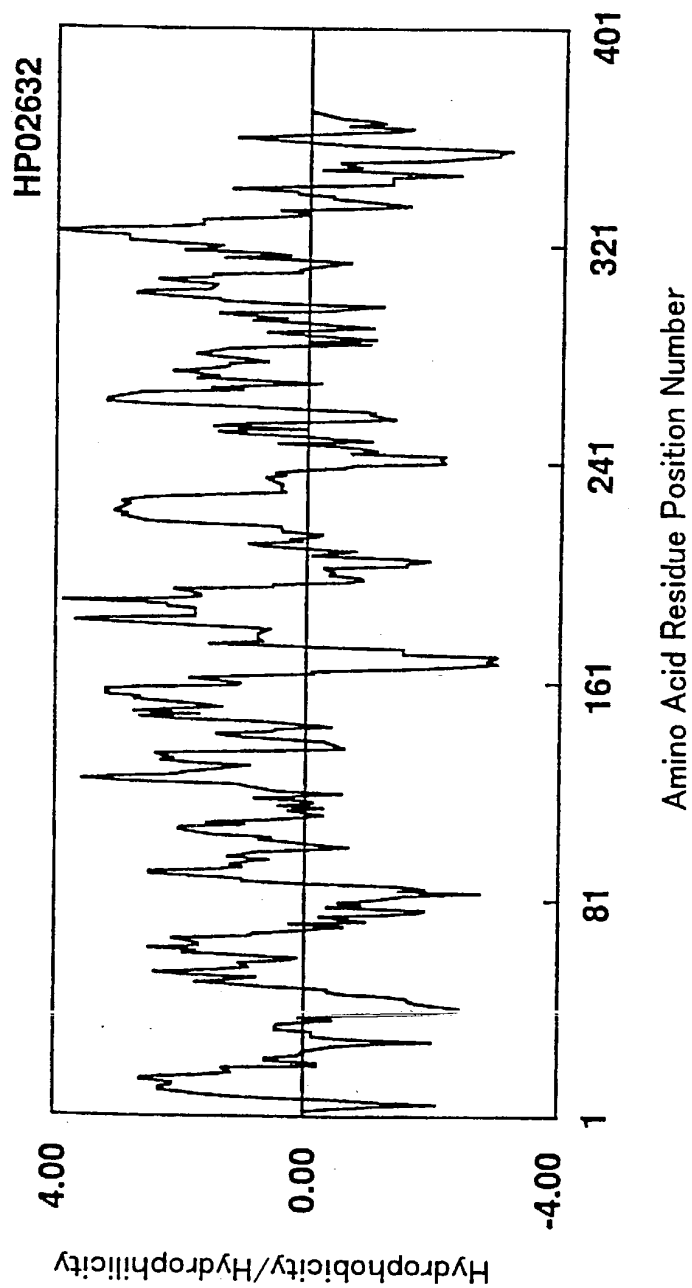


Fig. 26

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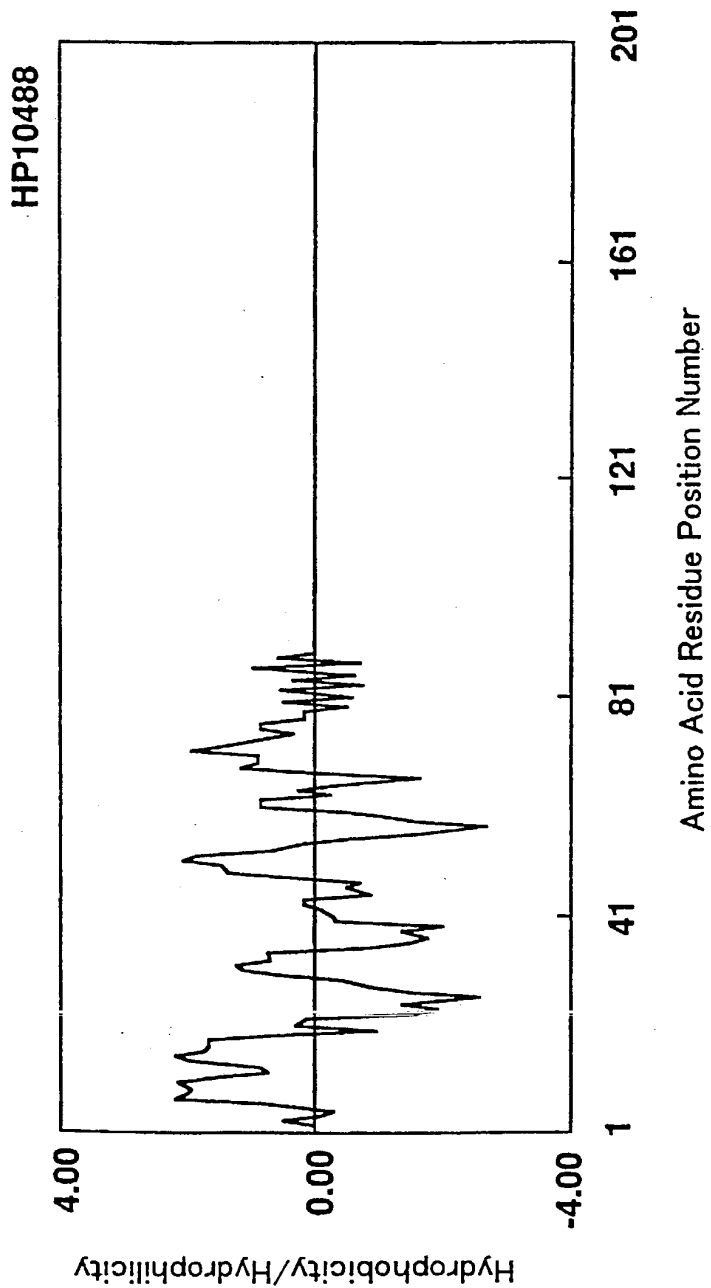


Fig.27

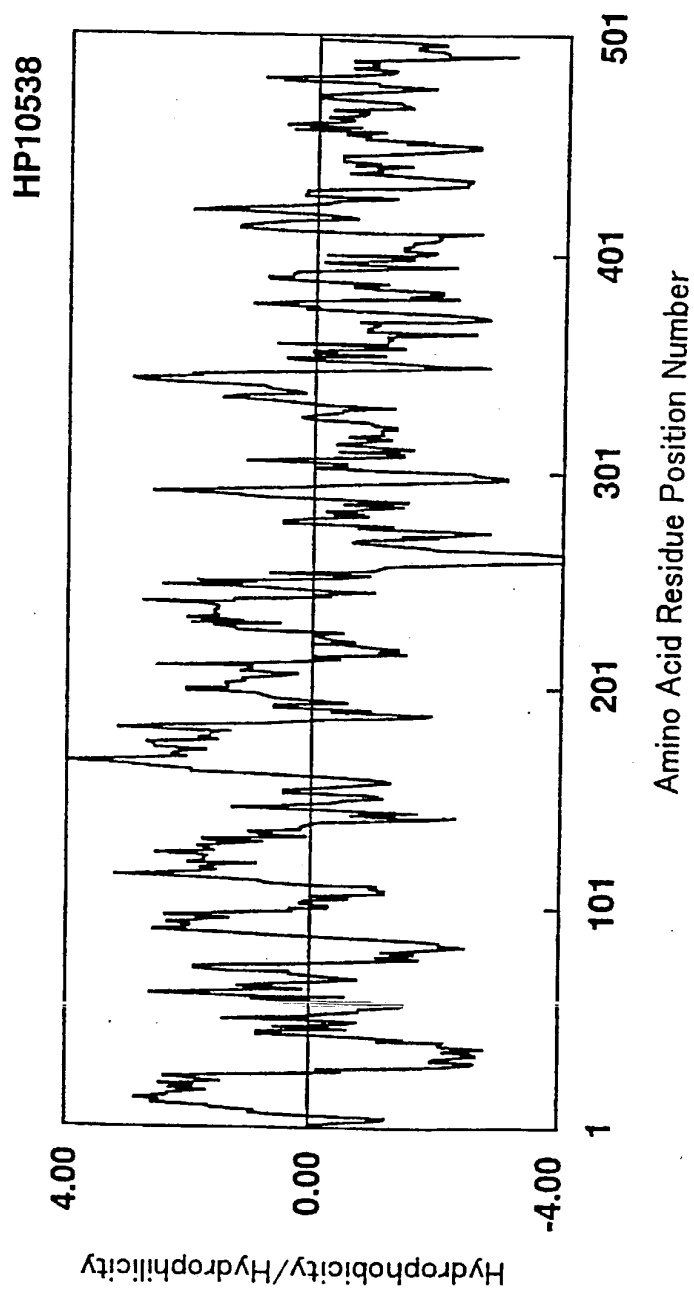


Fig. 28

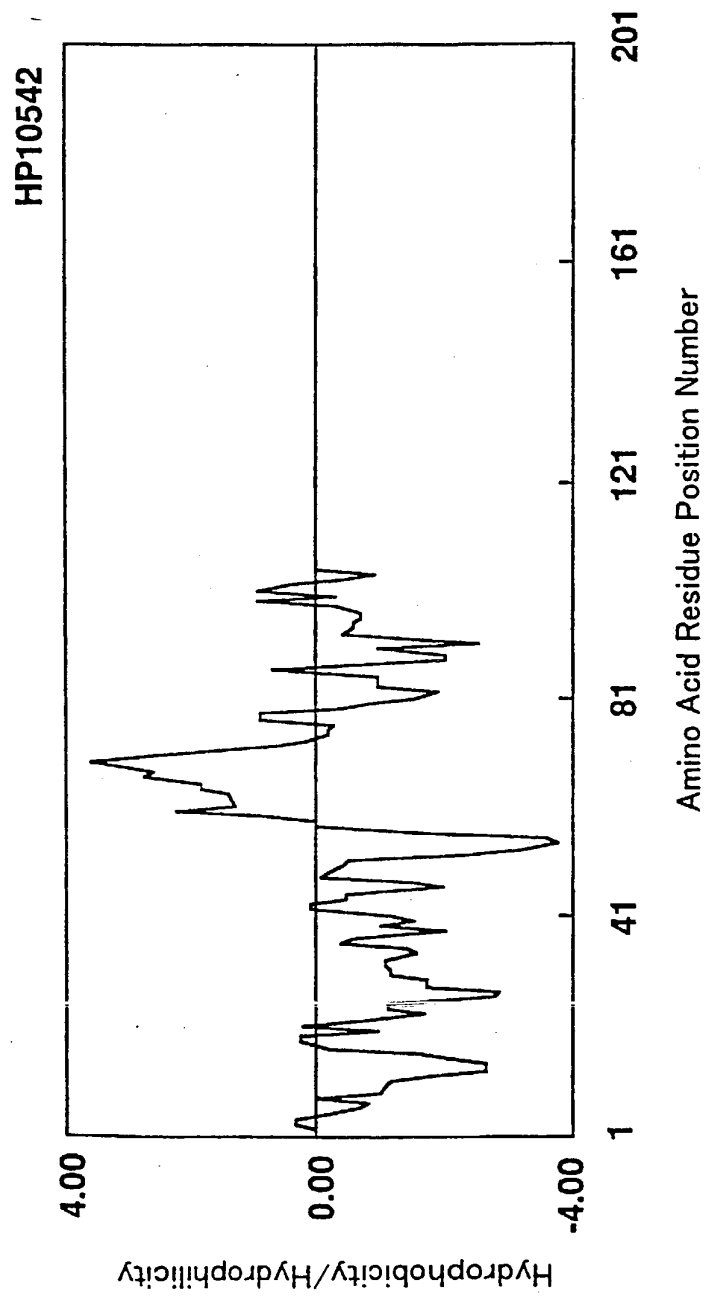


Fig. 29

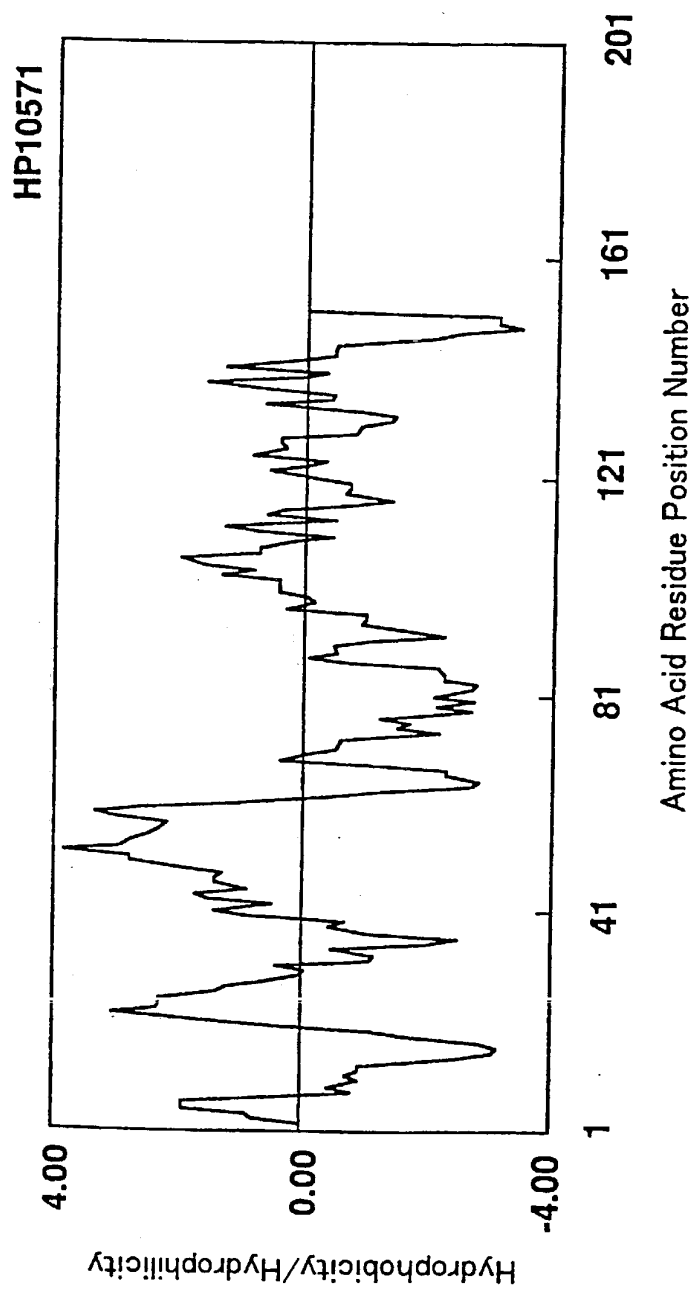


Fig. 30

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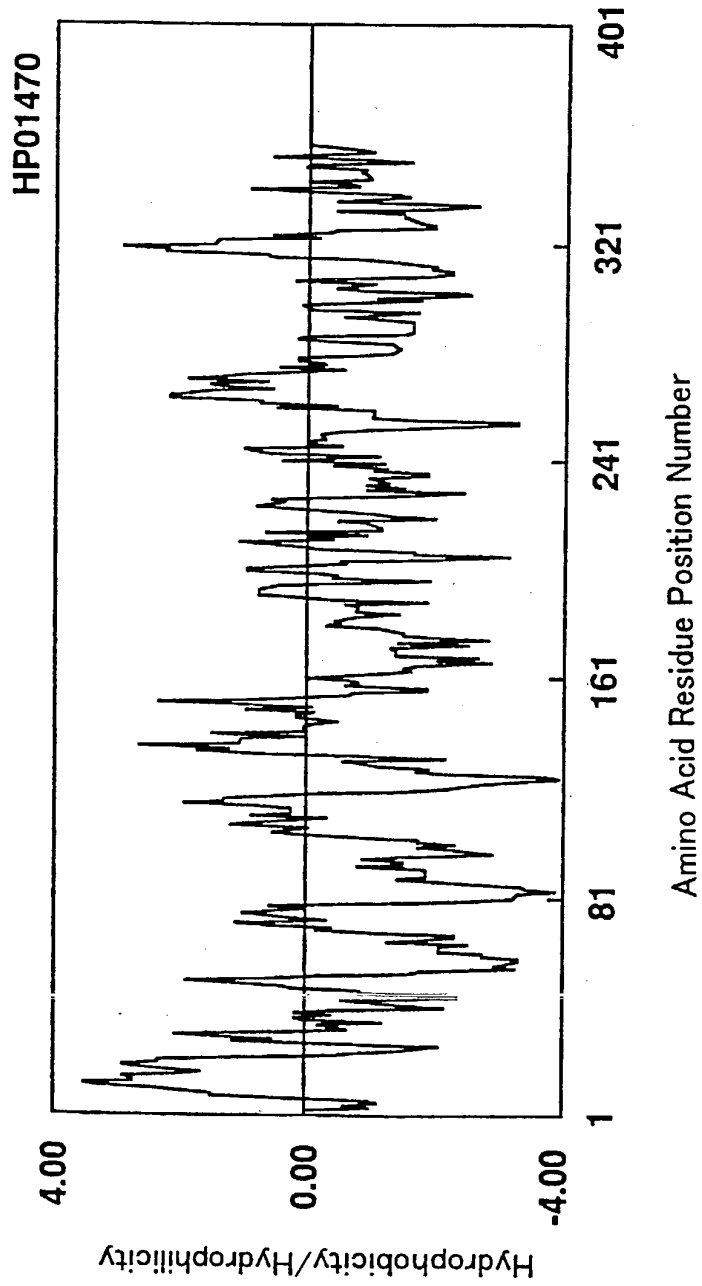


Fig. 31

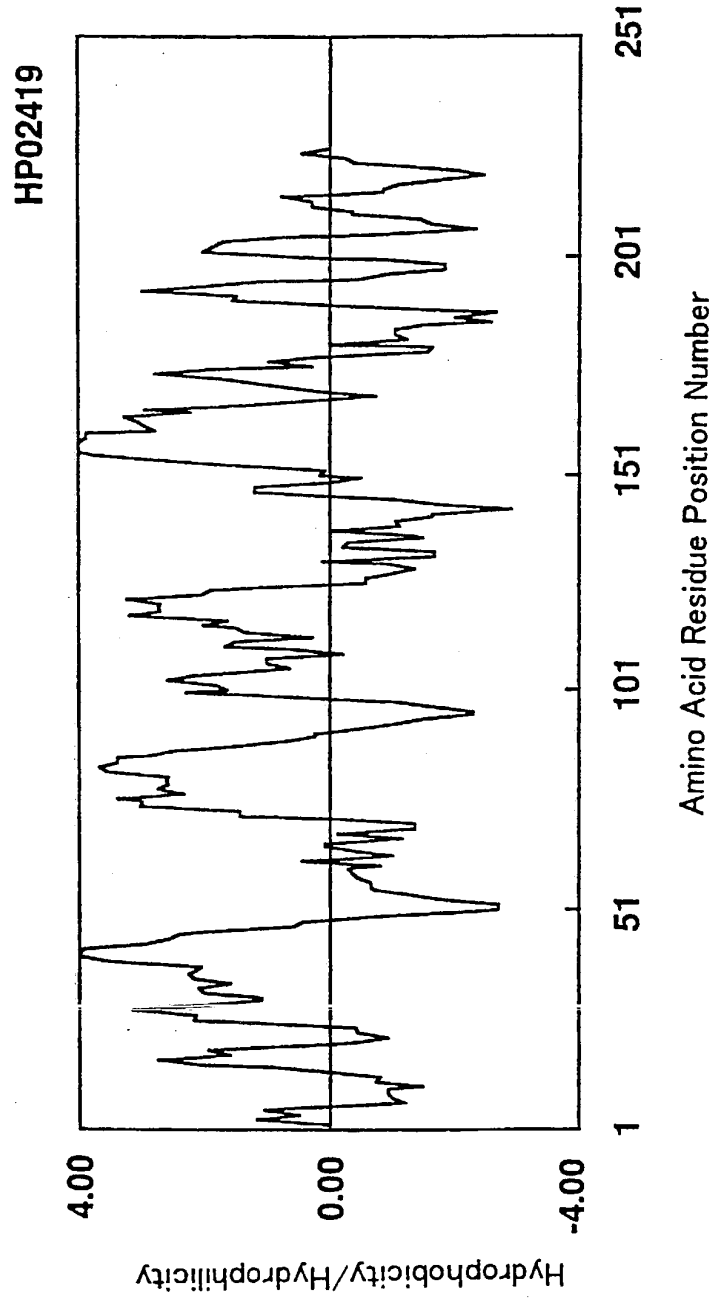


Fig.32

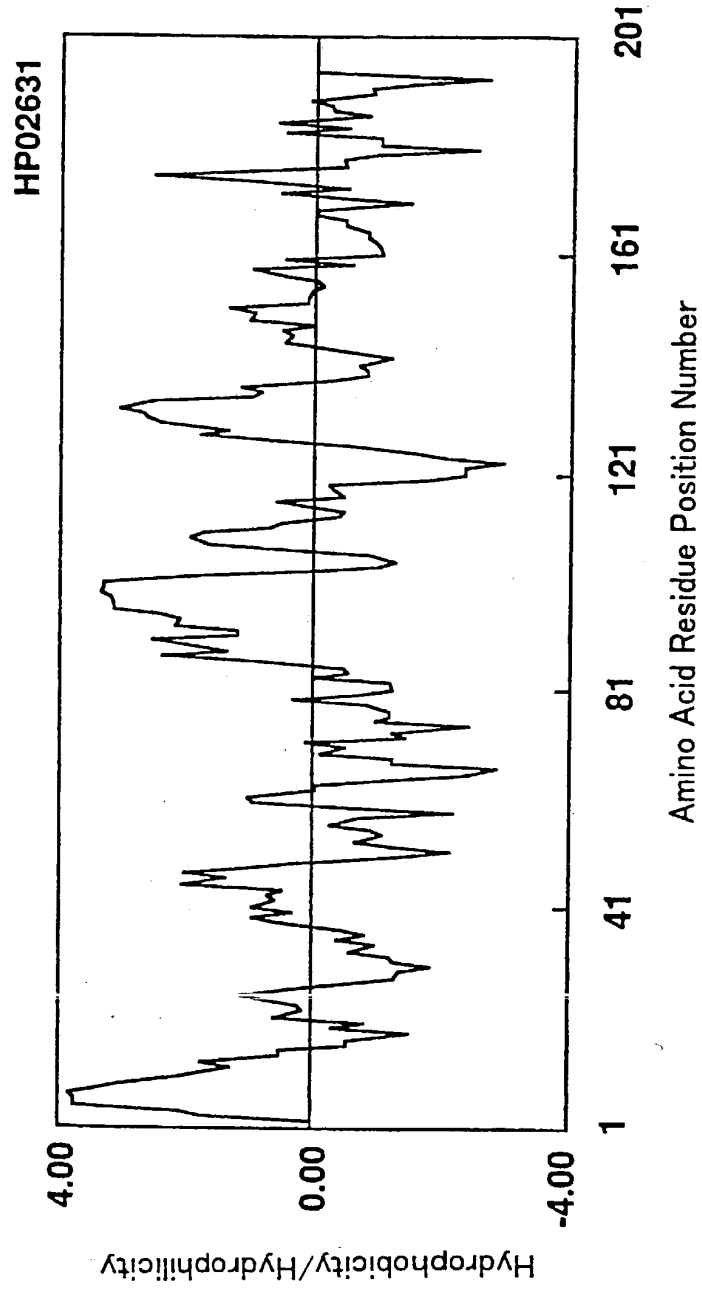


Fig. 33

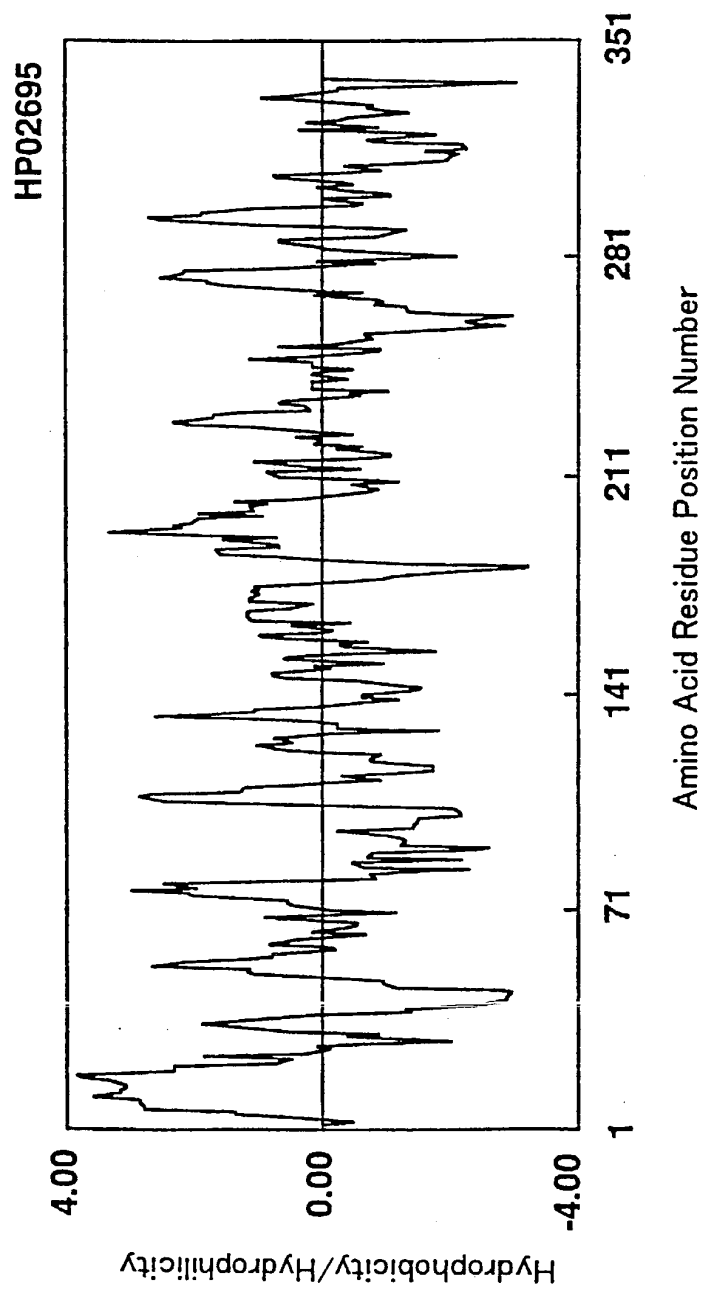


Fig. 34

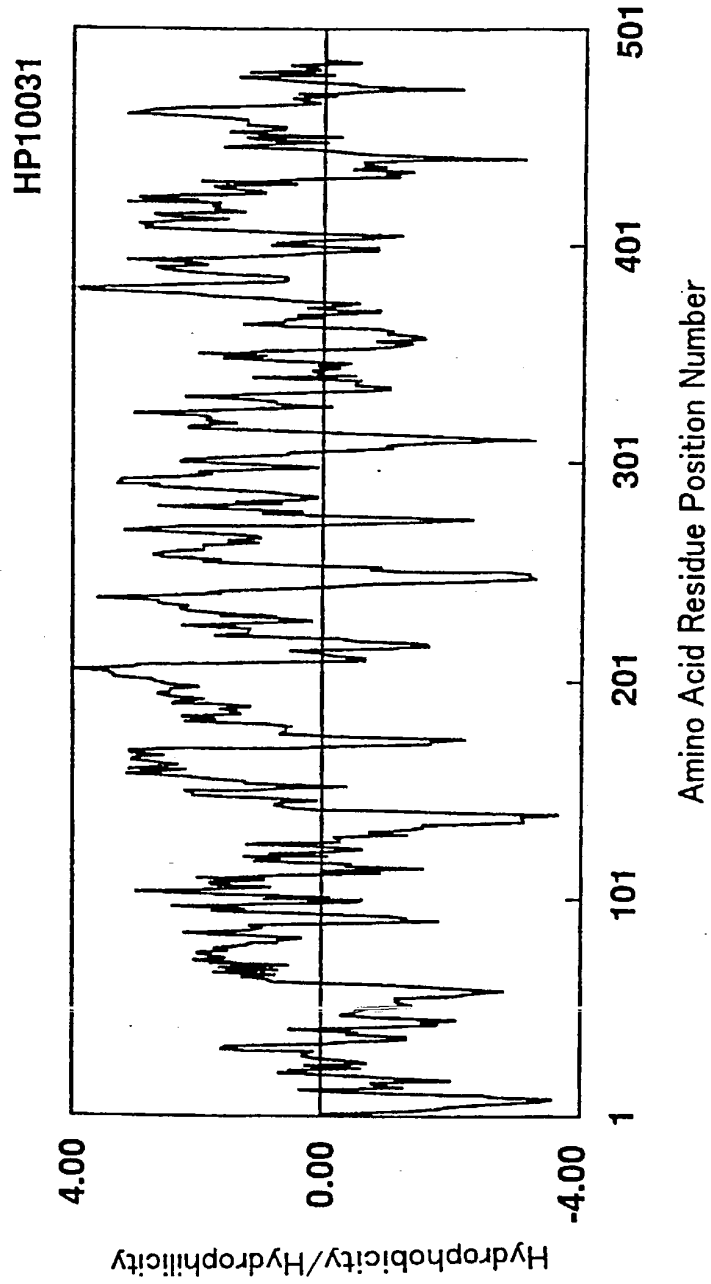


Fig. 35

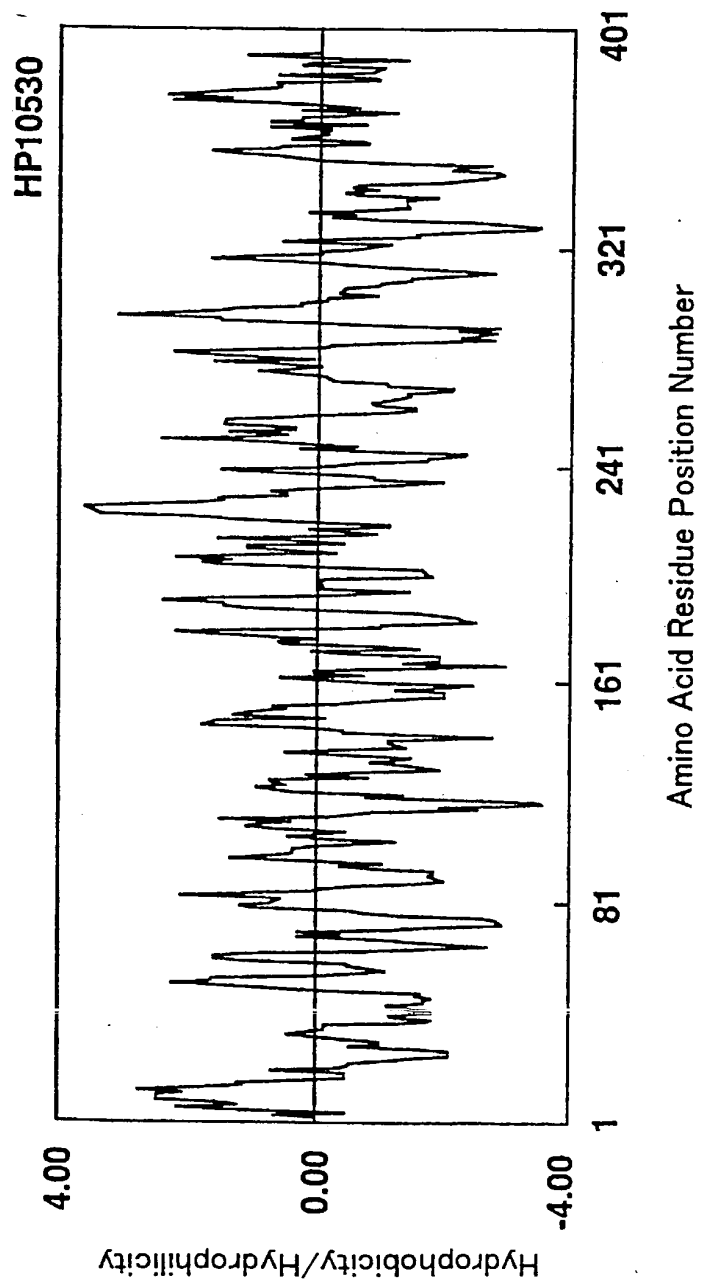


Fig. 36

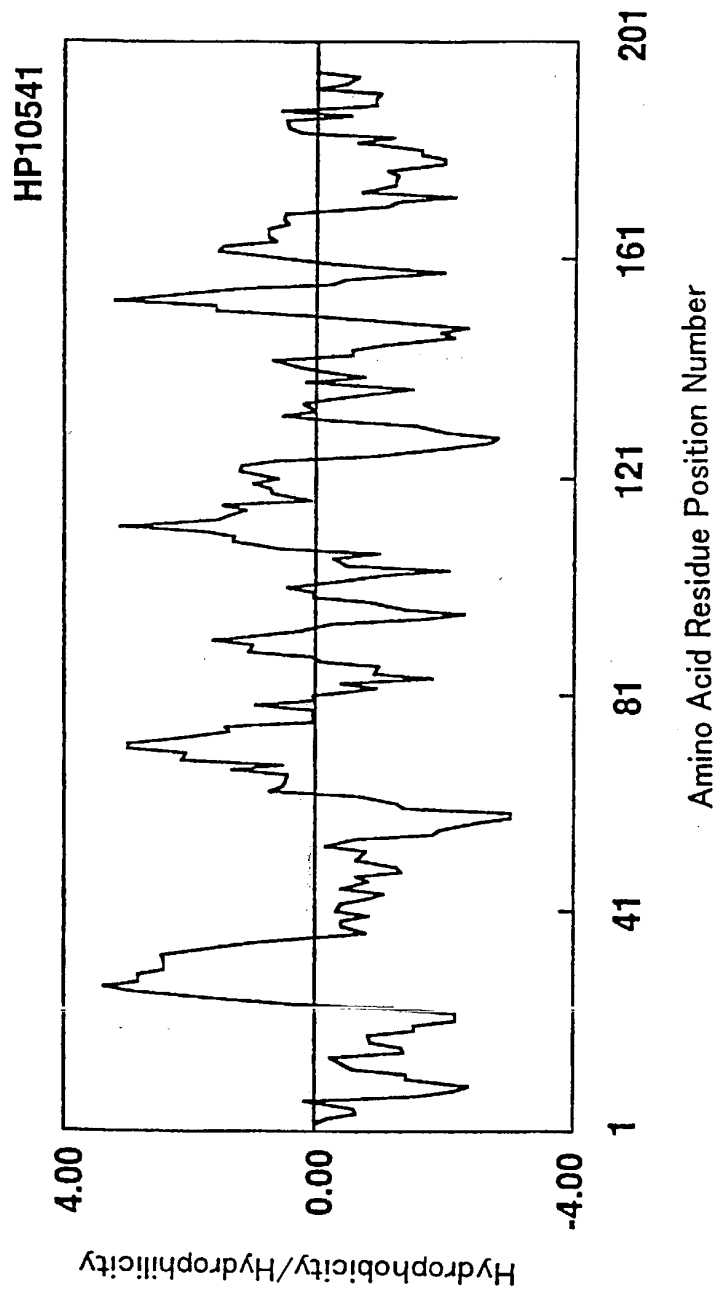


Fig.37

09/743247

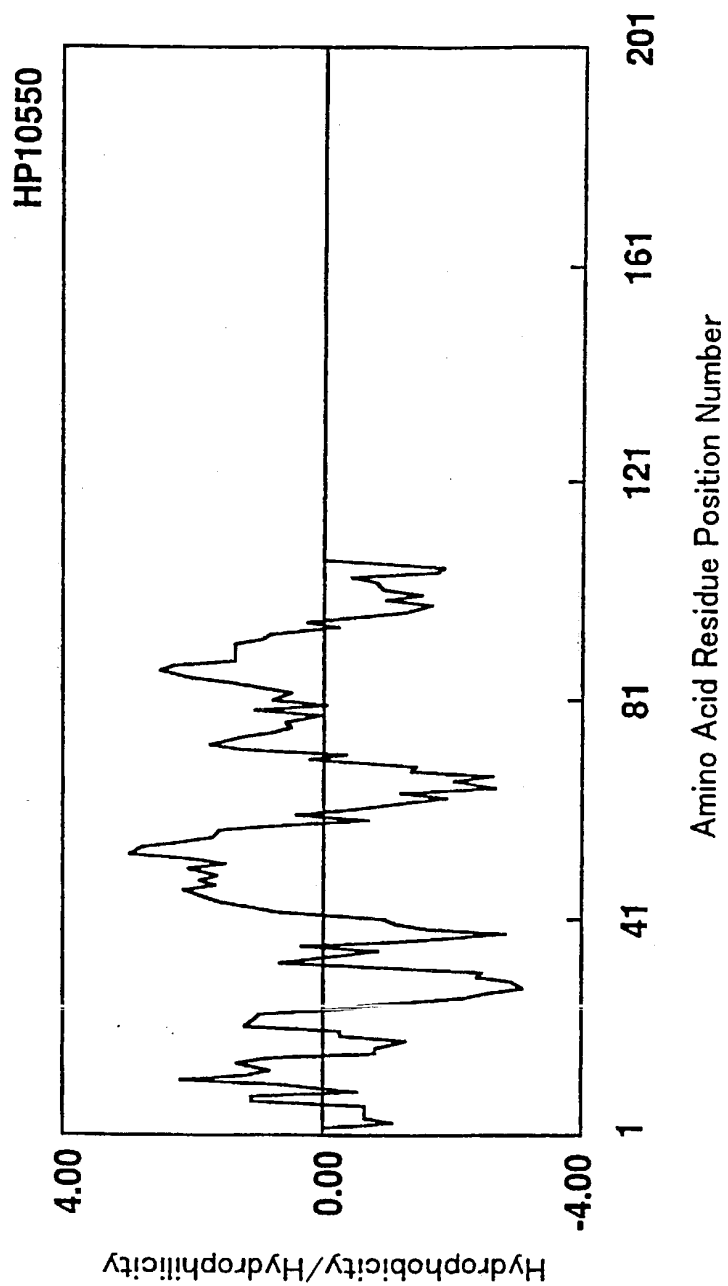


Fig. 38

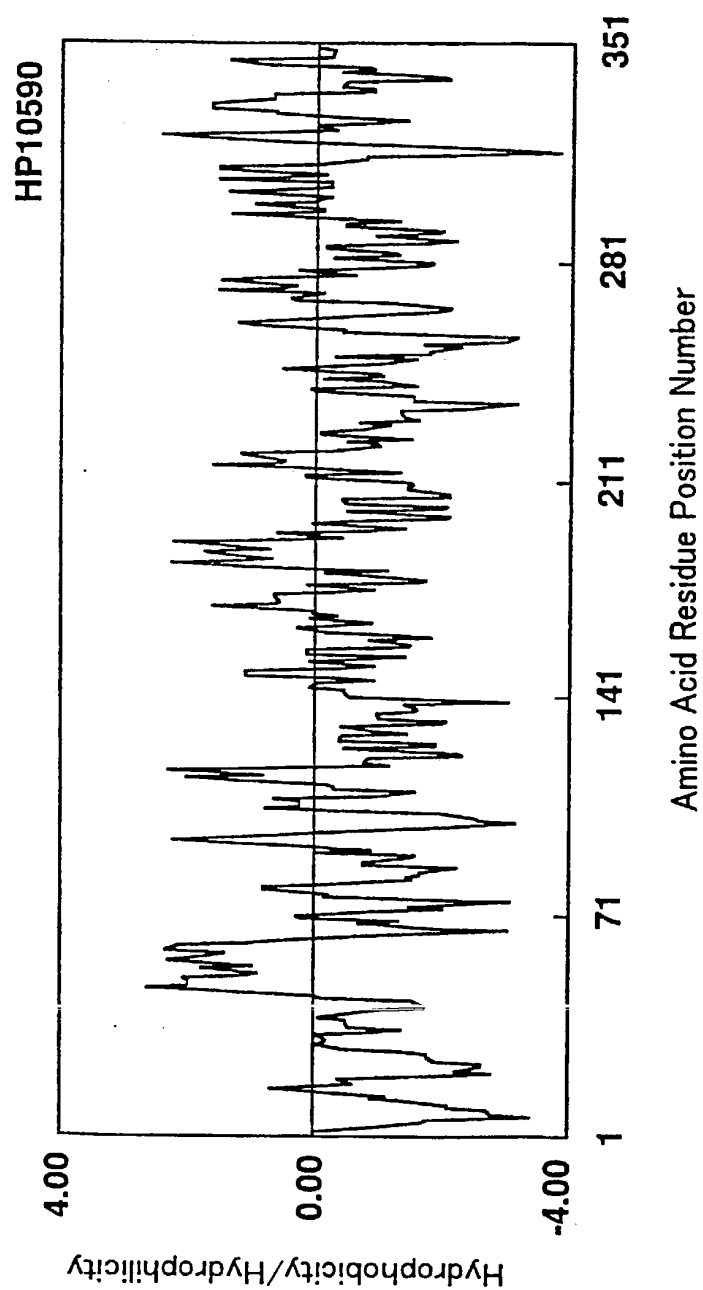


Fig. 39

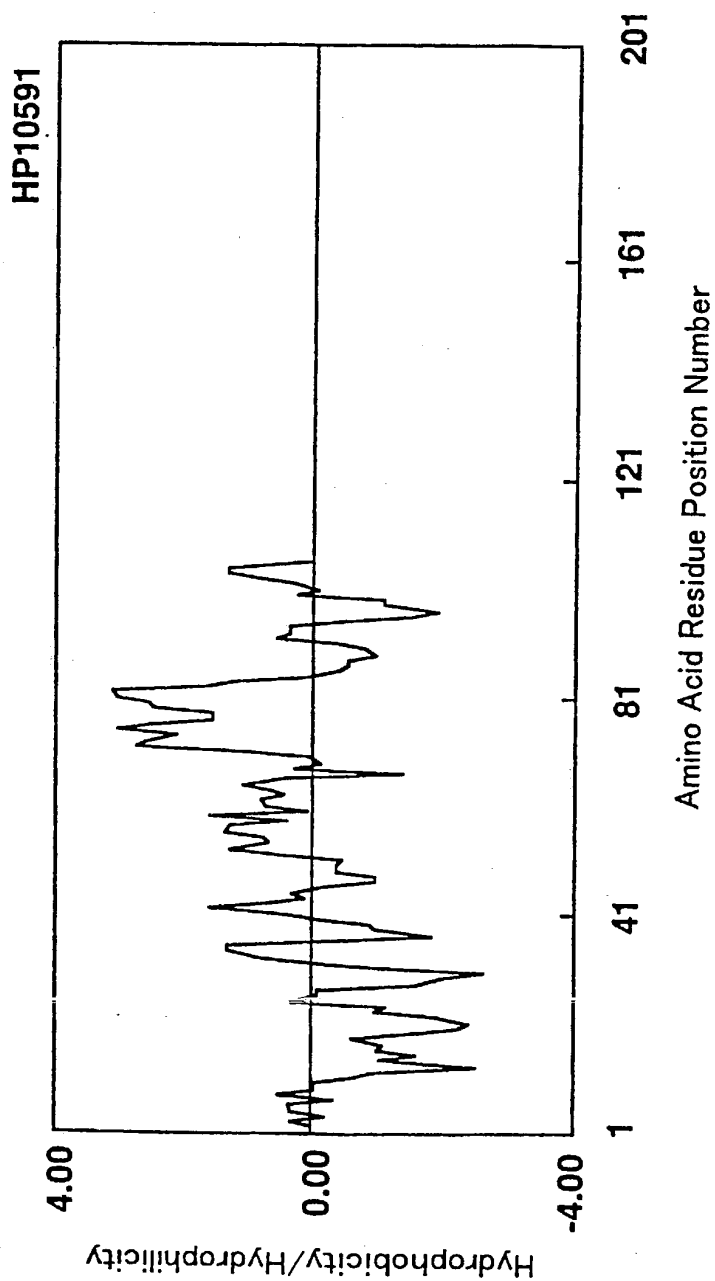


Fig. 40

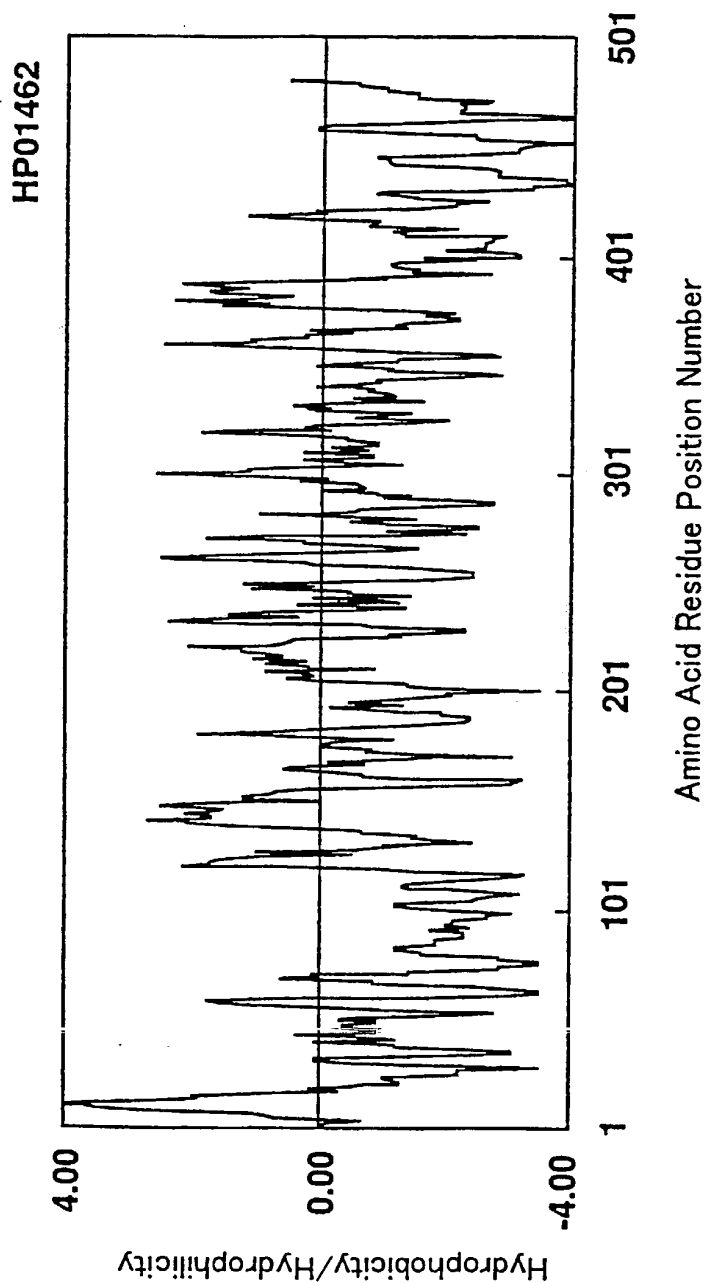


Fig. 41

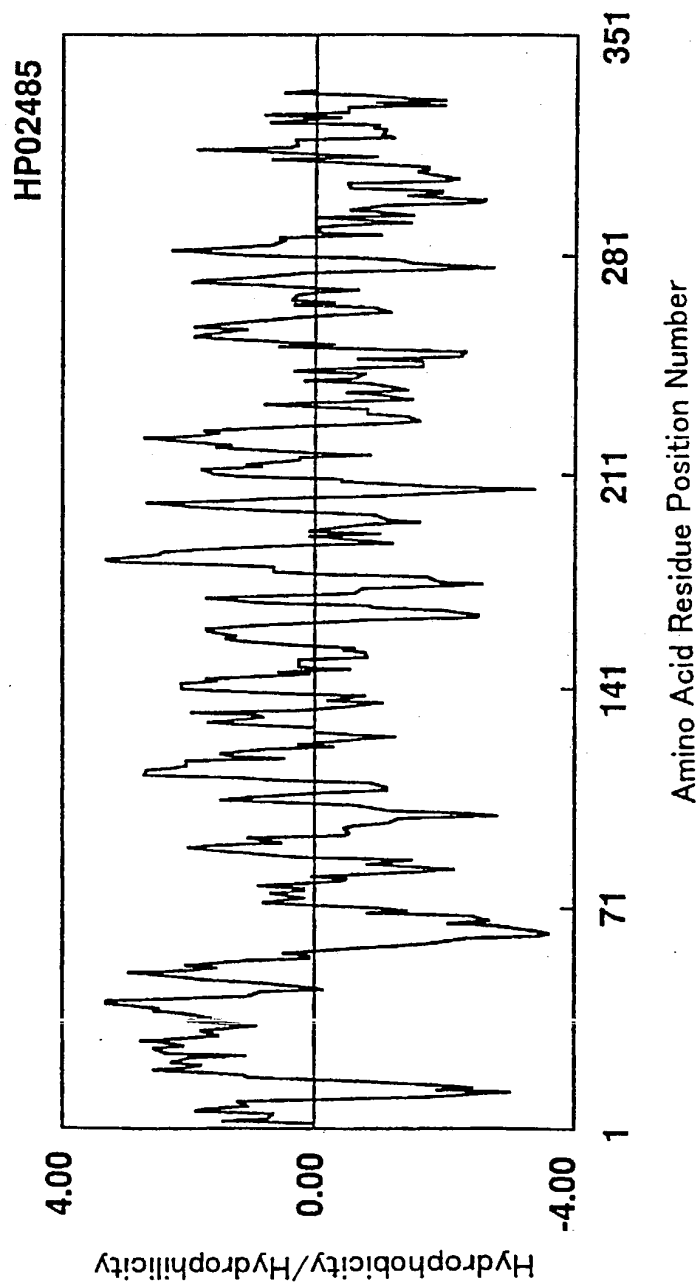


Fig.42

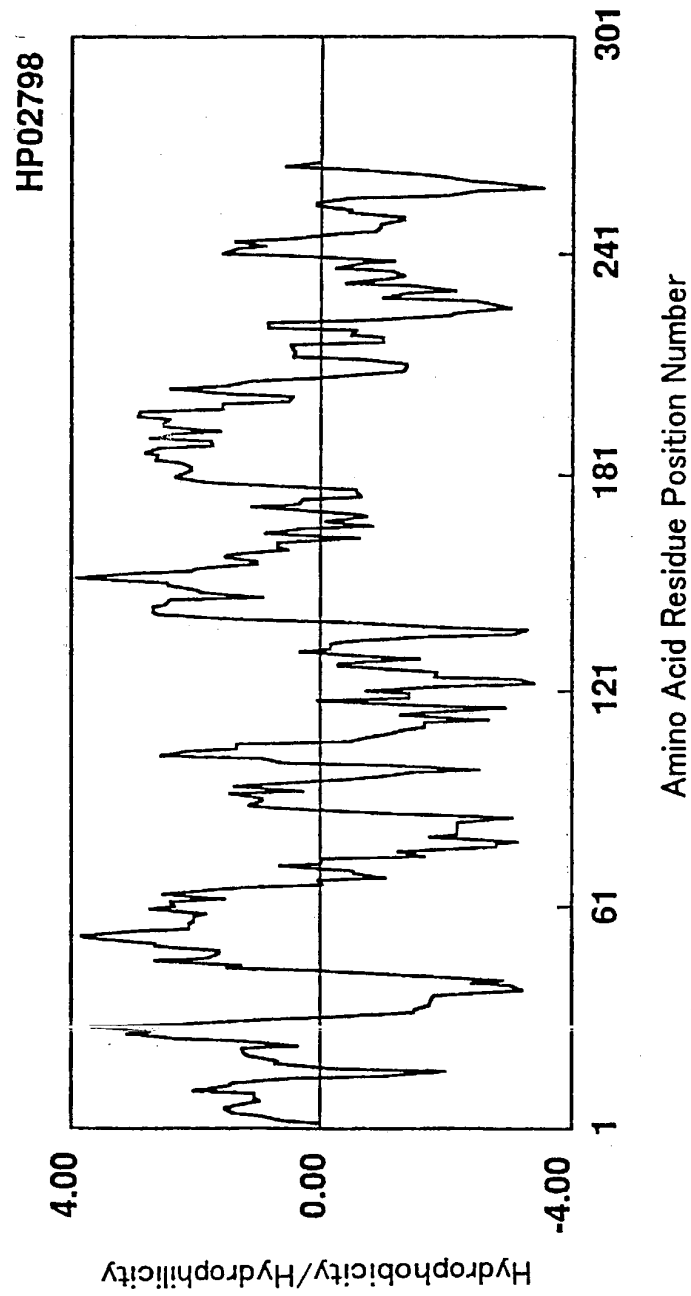


Fig. 43

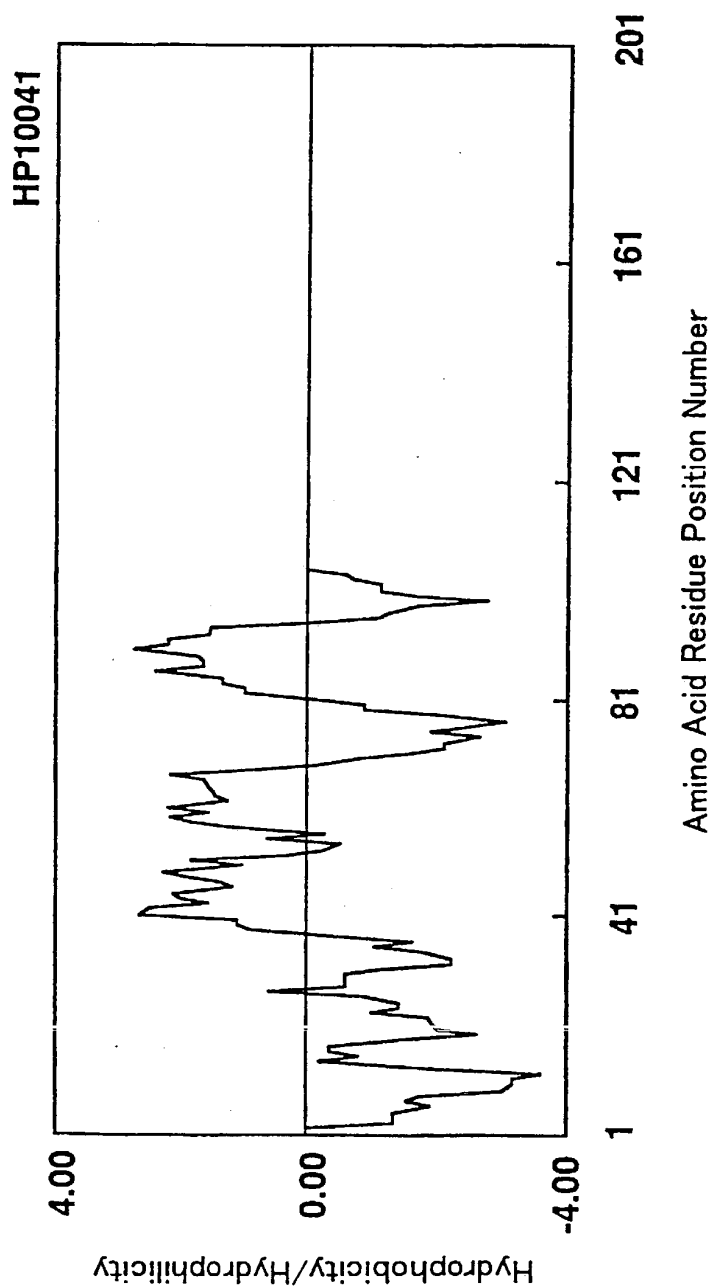


Fig. 44

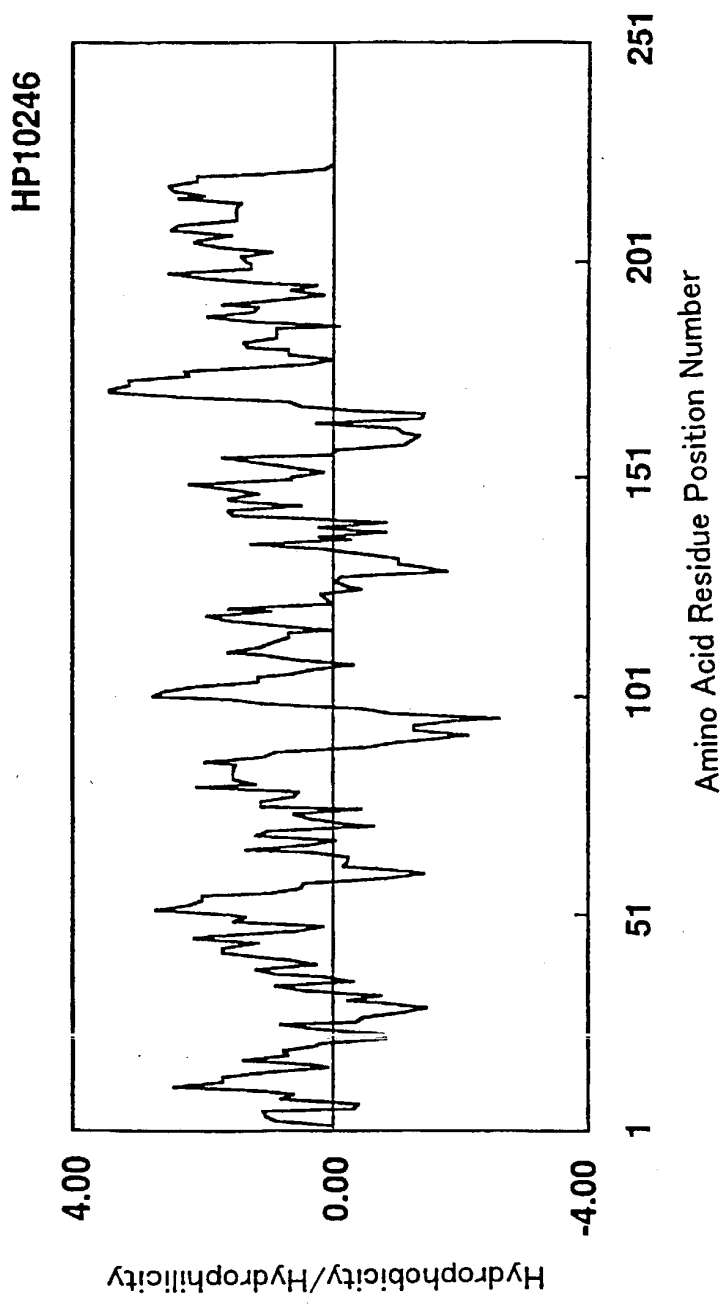


Fig. 45

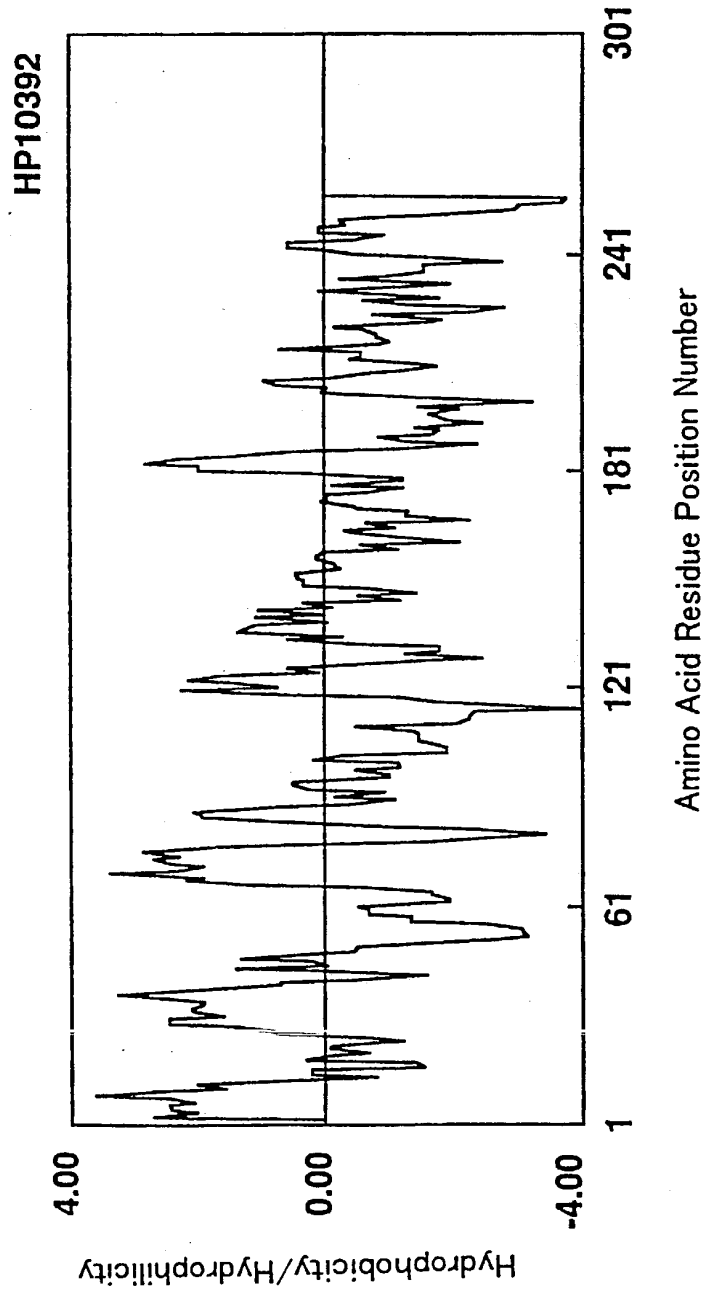


Fig. 46

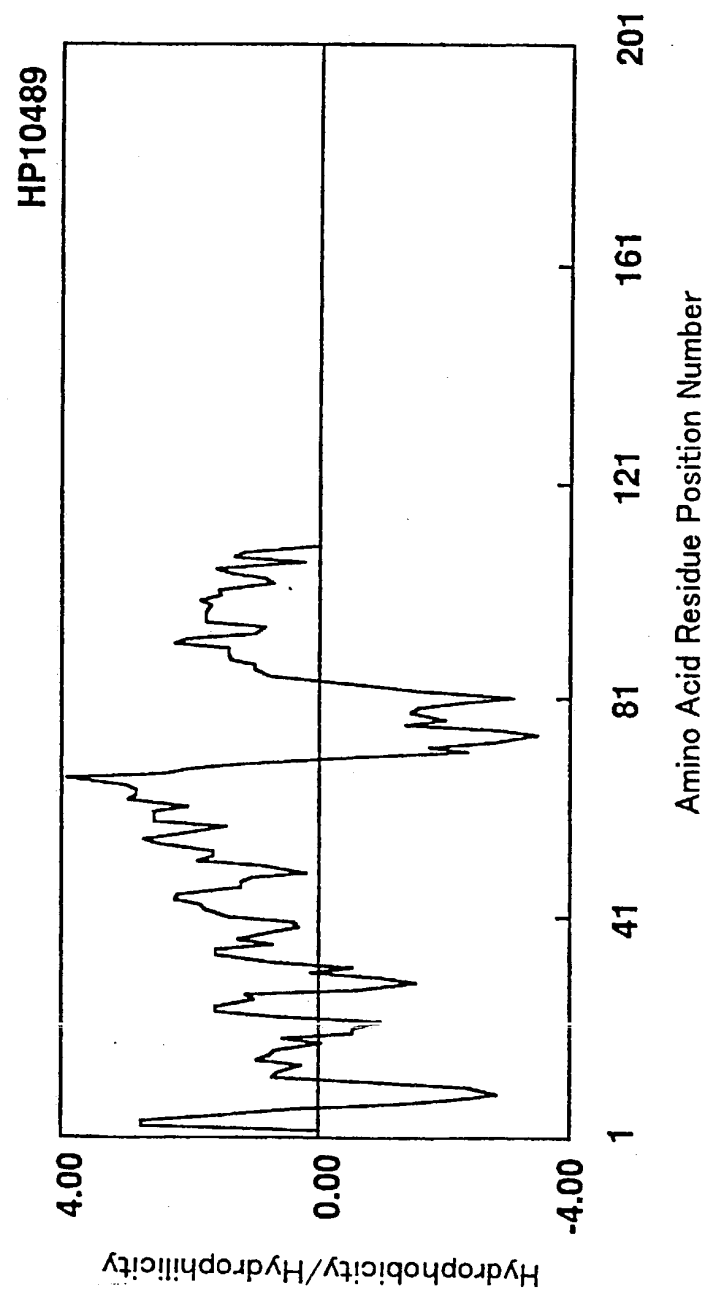


Fig.47

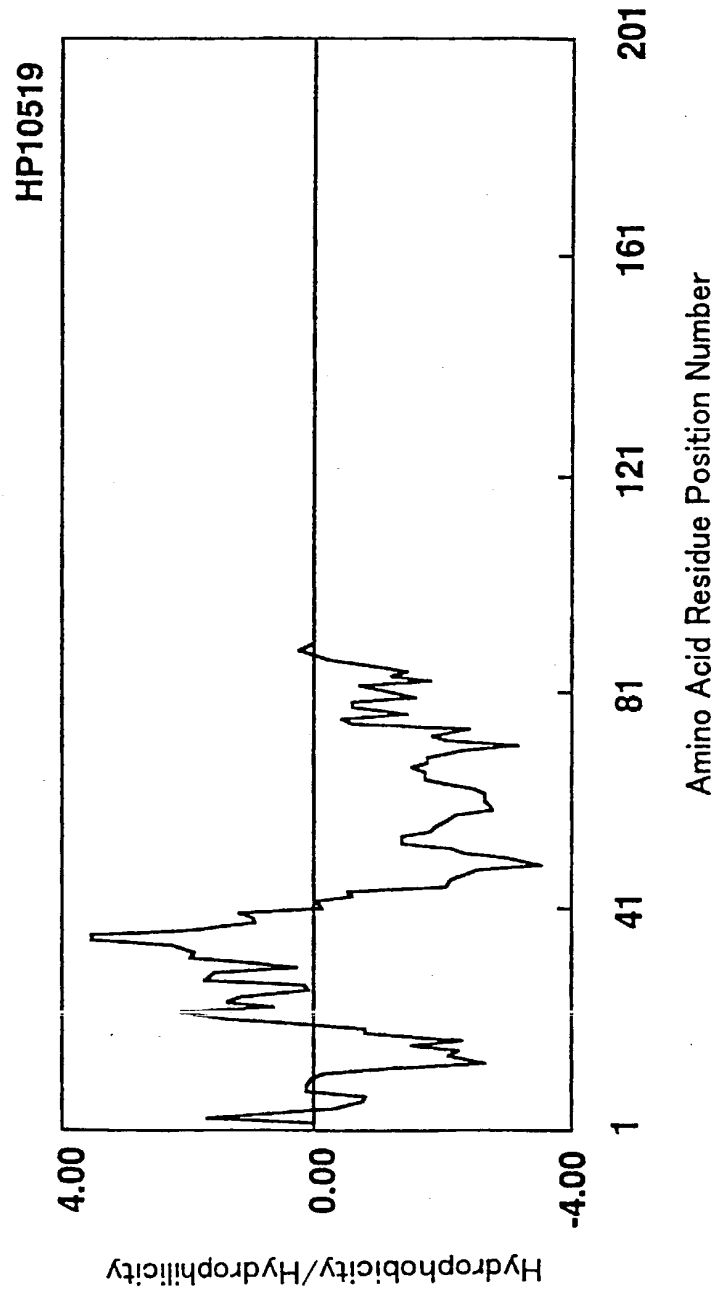


Fig. 48

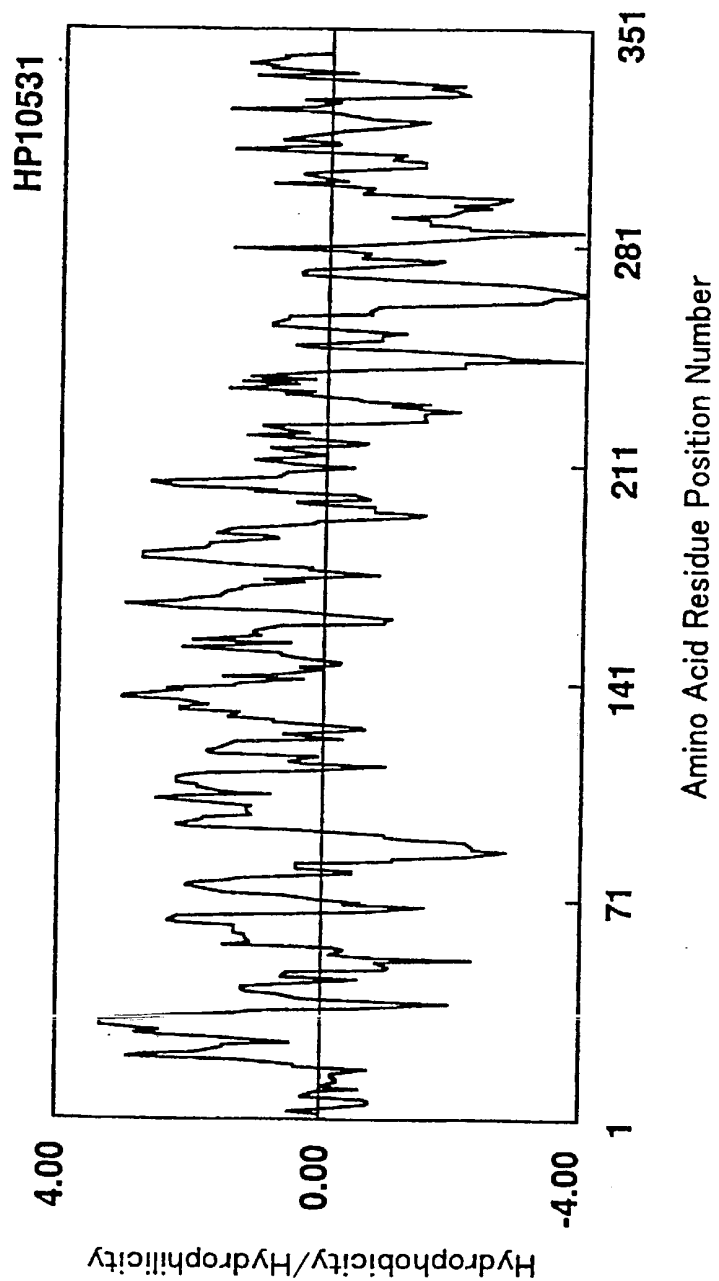


Fig. 49

50/50

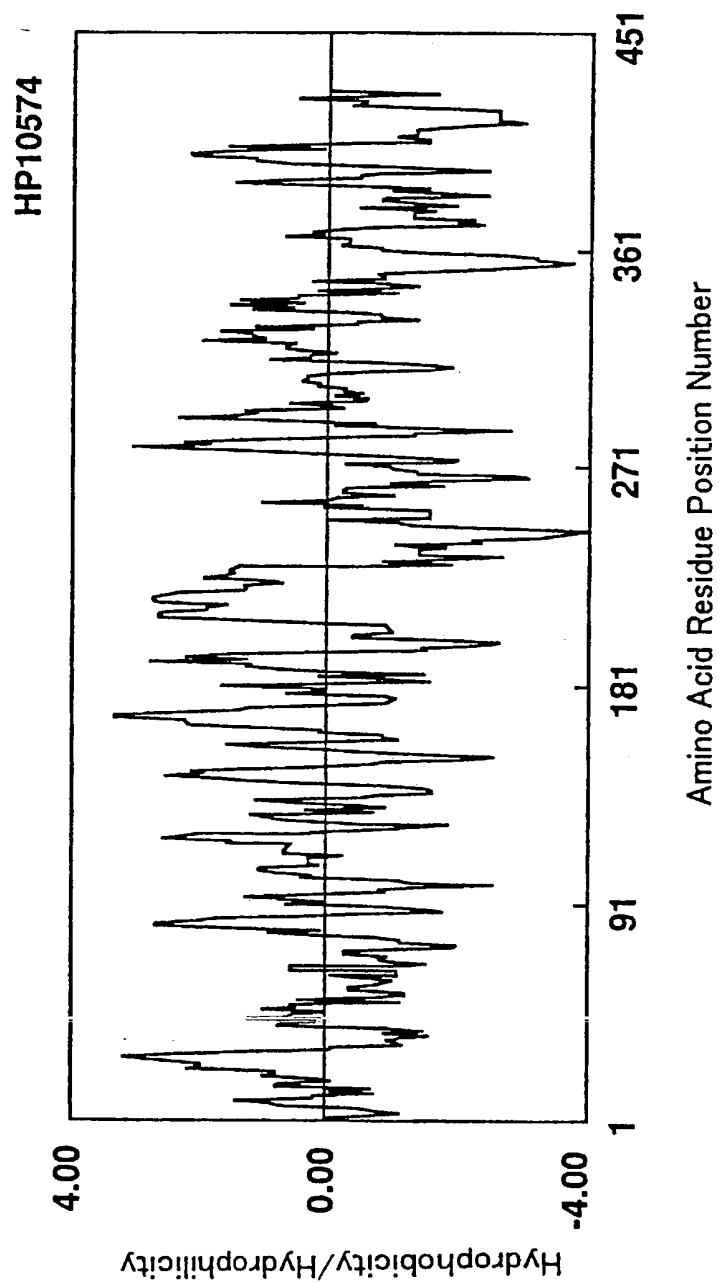


Fig. 50

Atty Docket No.: GIN-6718CP5US

**DECLARATION, PETITION AND POWER OF ATTORNEY
FOR PATENT APPLICATION**

(Check one):

- ☐ Declaration Submitted with Initial Filing
☒ Declaration Submitted after Initial Filing

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

**HUMAN PROTEINS HAVING HYDROPHOBIC DOMAINS
AND DNAs ENCODING THESE PROTEINS**

the specification of which (check one):

- ☐ is attached hereto.
OR
☒ was filed on 5 January 2001 as U.S. National Application Serial No. 09/743,247
(U.S. National Filing of PCT/JP99/03929 filed on 22 July 1999).
- ☐ and was amended by PCT Article 19 Amendment on _____
(if applicable),
- ☐ and was amended by PCT Article 34 Amendment on _____
(if applicable).

I acknowledge the duty to disclose to the Office all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, §1.56.

I hereby state that I have reviewed and understood the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

PRIORITY CLAIM

(Check one):

- ☐ no such applications have been filed.
- ☒ such applications have been filed as follows

1) FOREIGN PRIORITY CLAIM: I hereby claim foreign priority benefits under Title 35, United States Code, §119(a)-(d) or §365(b) of any foreign application(s) for patent or inventor's certificate or §365(a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate or any PCT international application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application Number(s)	Country	Foreign Filing Date (dd/mm/yyyy)	Priority Not Claimed	Certified Copy Attached	
				Yes	No
10/275505	JP	29/09/1998	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
10/254736	JP	09/09/1998	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
10/238116	JP	25/08/1998	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
10/224105	JP	07/08/1998	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
10/208820	JP	24/07/1998	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>

- ☐ Additional foreign application numbers are listed on a supplemental priority sheet attached hereto.

2) PROVISIONAL PRIORITY CLAIM: I hereby claim the benefit under Title 35, United States Code §119(e) of any United States provisional application(s) listed below.

Provisional Application Number(s)	Filing Date (dd/mm/yyyy)

- ☐ Additional provisional application numbers are listed on a supplemental priority sheet attached hereto.

3) U.S./PCT PRIORITY CLAIM: I hereby claim the benefit under Title 35, United States Code, §120 of any United States application or §365(c) of any PCT international application designating the United States of America, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT international application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose information which is known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application.

POWER OF ATTORNEY:

As a named inventor, I hereby appoint the following attorneys and/or agents to prosecute this application and transact all business in the Patent and Trademark Office connected therewith.

James E. Cockfield	Reg. No. <u>19,162</u>	Peter C. Lauro	Reg. No. <u>32,360</u>
Thomas V. Smurzynski	Reg. No. <u>24,798</u>	DeAnn F. Smith	Reg. No. <u>36,683</u>
Ralph A. Loren	Reg. No. <u>29,325</u>	David J. Rikkers	Reg. No. <u>43,882</u>
Giulio A. DeConti, Jr.	Reg. No. <u>31,503</u>	Chi Suk Kim	Reg. No. <u>42,728</u>
Ann Lamport Hammitte	Reg. No. <u>34,858</u>	Maria Laccotripe Zacharakis	Limited Recognition Under 37 C.F.R. § 10.9(b)
Elizabeth A. Hanley	Reg. No. <u>33,505</u>		
Amy E. Mandragouras	Reg. No. <u>36,207</u>	Debra J. Milasincic	Reg. No. <u>46,931</u>
Anthony A. Laurentano	Reg. No. <u>38,220</u>	David R. Burns	Reg. No. <u>46,590</u>
Jane E. Remillard	Reg. No. <u>38,872</u>	Sean D. Detweiler	Reg. No. <u>42,482</u>
Jeremiah Lynch	Reg. No. <u>17,425</u>	Peter S. Stecher	Reg. No. <u>47,259</u>
Kevin J. Canning	Reg. No. <u>35,470</u>	Adam M. Goodmann	Reg. No. <u>43,640</u>
Jeanne M. DiGiorgio	Reg. No. <u>41,710</u>	Cynthia L. Kanik	Reg. No. <u>37,320</u>
Megan E. Williams	Reg. No. <u>43,270</u>		
Nicholas P. Triano III	Reg. No. <u>36,397</u>		

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Barbara A. Gyure	Reg. No. <u>34,614</u>	Elizabeth A. Hurley	Reg. No. <u>41,859</u>

of GENETICS INSTITUTE, INC., 87 CambridgePark Drive, Cambridge, Massachusetts 02140, United States of America,

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Gale F. Matthews	Reg. No. <u>32,269</u>	Alan M. Gordon	Reg. No. <u>30,637</u>
Darryl L. Webster	Reg. No. <u>34,276</u>		

of GENETICS INSTITUTE, INC., One Campus Drive, Parsippany, New Jersey 07054, United States of America, and

Rebecca R. Barrett	Reg. No. <u>35,152</u>	Steven R. Eck	Reg. No. <u>36,126</u>
Arnold S. Milowsky	Reg. No. <u>35,288</u>	Michael R. Nagy	Reg. No. <u>33,432</u>
George Tarnowski	Reg. No. <u>27,472</u>		

of GENETICS INSTITUTE, INC., P.O. Box 8299, Philadelphia, Pennsylvania 19101, United States of America.

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Send Correspondence to: Amy E. Mandragouras, Esq., Lahive & Cockfield, LLP, 28 State Street, Boston, Massachusetts 02109, United States of America

Direct Telephone Calls to: Amy E. Mandragouras, Esq., (617) 227-7400, Lahive & Cockfield, LLP, 28 State Street, Boston, Massachusetts 02109, United States of America

U.S. Parent Application Number	PCT Parent Number	Parent Filing Date (dd/mm/yyyy)	Parent Patent Number (if applicable)
	PCT/JP99/03929	22 July 1999 (22.07.99)	

☐ Additional U.S. or PCT international application numbers are listed on a supplemental priority sheet attached hereto.



ENTERED

PCT09

RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/743,247A

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TIME: 14:43:12

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W--> 4 Proteins

W--> 5 <130> FILE REFERENCE: 1997.13300

W--> 6 <140> CURRENT APPLICATION NUMBER: US/09/743,247A

7 <141> CURRENT FILING DATE: 1999-07-22

8 <150> PRIOR APPLICATION NUMBER: JP 10-208820

9 <151> PRIOR FILING DATE: 1998-07-24

10 <150> PRIOR APPLICATION NUMBER: JP 10-224105

11 <151> PRIOR FILING DATE: 1998-08-07

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13 <151> PRIOR FILING DATE: 1998-08-25

14 <150> PRIOR APPLICATION NUMBER: JP 10-254736

15 <151> PRIOR FILING DATE: 1998-09-09

16 <150> PRIOR APPLICATION NUMBER: JP 10-275505

17 <151> PRIOR FILING DATE: 1998-09-29

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23 <213> ORGANISM: Homo sapiens

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26 1 5 10 15

27 Gly Arg Ala Phe Ala Arg Ala Leu Arg Gln Glu Phe Ala Ala Ser Arg

28 20 25 30

29 Ala Ala Ala Asp Ala Arg Gly Arg Ala Gly His Arg Ser Ala Ala Ala

30 35 40 45

31 Ser Asn Leu Ser Gly Leu Ser Leu Gln Glu Ala Gln Ile Leu Asn

32 50 55 60

33 Val Ser Lys Leu Ser Pro Glu Glu Val Gln Lys Asn Tyr Glu His Leu

34 65 70 75 80

35 Phe Lys Val Asn Asp Lys Ser Val Gly Gly Ser Phe Tyr Leu Gln Ser

36 85 90 95

37 Lys Val Val Arg Ala Lys Glu Arg Leu Asp Glu Glu Leu Lys Ile Gln

38 100 105 110

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41 <210> SEQ ID NO: 2

42 <211> LENGTH: 131

43 <212> TYPE: PRT

44 <213> ORGANISM: Homo sapiens

RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/743,247A

DATE: 11/19/2002

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48 Gly Leu Met Phe Leu Met Leu Gly Cys Ala Leu Pro Ile Tyr Asn Lys
49           20           25           30
50 Tyr Trp Pro Leu Phe Val Leu Phe Tyr Ile Leu Ser Pro Ile Pro
51           35           40           45
52 Tyr Cys Ile Ala Arg Arg Leu Val Asp Asp Thr Asp Ala Met Ser Asn
53           50           55           60
54 Ala Cys Lys Glu Leu Ala Ile Phe Leu Thr Thr Gly Ile Val Val Ser
55           65           70           75           80
56 Ala Phe Gly Leu Pro Ile Val Phe Ala Arg Ala His Leu Ile Glu Trp
57           85           90           95
58 Gly Ala Cys Ala Leu Val Leu Thr Gly Asn Thr Val Ile Phe Ala Thr
59           100          105          110
60 Ile Leu Gly Phe Phe Leu Val Phe Gly Ser Asn Asp Asp Phe Ser Trp
61           115          120          125
62 Gln Gln Trp
63           130

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64 <210> SEQ ID NO: 3

65 <211> LENGTH: 242

66 <212> TYPE: PRT

67 <213> ORGANISM: Homo sapiens

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71 Lys Phe Lys Gly Pro Phe Thr Asp Val Val Thr Thr Asn Leu Lys Leu
72           20           25           30
73 Arg Asn Pro Ser Asp Arg Lys Val Cys Phe Lys Val Lys Thr Thr Ala
74           35           40           45
75 Pro Arg Arg Tyr Cys Val Arg Pro Asn Ser Gly Ile Ile Asp Pro Gly
76           50           55           60
77 Ser Thr Val Thr Val Ser Val Met Leu Gln Pro Phe Asp Tyr Asp Pro
78           65           70           75           80
79 Asn Glu Lys Ser Lys His Lys Phe Met Val Gln Thr Ile Phe Ala Pro
80           85           90           95
81 Pro Asn Thr Ser Asp Met Glu Ala Val Trp Lys Glu Ala Lys Pro Asp
82           100          105          110
83 Glu Leu Met Asp Ser Lys Leu Arg Cys Val Phe Glu Met Pro Asn Glu
84           115          120          125
85 Asn Asp Lys Leu Asn Asp Met Glu Pro Ser Lys Ala Val Pro Leu Asn
86           130          135          140
87 Ala Ser Lys Gln Asp Gly Pro Met Pro Lys Pro His Ser Val Ser Leu
88           145          150          155          160
89 Asn Asp Thr Glu Thr Arg Lys Leu Met Glu Glu Cys Lys Arg Leu Gln
90           165          170          175
91 Gly Glu Met Met Lys Leu Ser Glu Glu Asn Arg His Leu Arg Asp Glu
92           180          185          190
93 Gly Leu Arg Leu Arg Lys Val Ala His Ser Asp Lys Pro Gly Ser Thr

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RAW SEQUENCE LISTING

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DATE: 11/19/2002

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95 Ser Thr Ala Ser Phe Arg Asp Asn Val Thr Ser Pro Leu Pro Ser Leu
96      210          215          220
97 Leu Val Val Ile Ala Ala Ile Phe Ile Gly Phe Phe Leu Gly Lys Phe
98 225          230          235          240
99 Ile Leu
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102 <212> TYPE: PRT
103 <213> ORGANISM: Homo sapiens
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106 1          5          10          15
107 Leu Leu Met Pro Ala Val Ser Val Gly Asn Val Gly Gln Leu Ala Met
108      20          25          30
109 Asp Leu Ile Ile Ser Thr Leu Asn Met Ser Lys Ile Gly Tyr Phe Tyr
110      35          40          45
111 Thr Asp Cys Leu Val Pro Met Val Gly Asn Asn Pro Tyr Ala Thr Thr
112      50          55          60
113 Glu Gly Asn Ser Thr Glu Leu Ser Ile Asn Ala Glu Val Tyr Ser Leu
114 65          70          75          80
115 Pro Ser Arg Lys Leu Val Ala Leu Gln Leu Arg Ser Ile Phe Ile Lys
116      85          90          95
117 Tyr Lys Ser Lys Pro Phe Cys Glu Lys Leu Leu Ser Trp Val Lys Ser
118      100          105          110
119 Ser Gly Cys Ala Arg Val Ile Val Leu Ser Ser Ser His Ser Tyr Gln
120      115          120          125
121 Arg Asn Asp Leu Gln Leu Arg Ser Thr Pro Phe Arg Tyr Leu Leu Thr
122      130          135          140
123 Pro Ser Met Gln Lys Ser Val Gln Asn Lys Ile Lys Ser Leu Asn Trp
124 145          150          155          160
125 Glu Glu Met Glu Lys Ser Arg Cys Ile Pro Glu Ile Asp Asp Ser Glu
126      165          170          175
127 Phe Cys Ile Arg Ile Pro Gly Gly Gly Ile Thr Lys Thr Leu Tyr Asp
128      180          185          190
129 Glu Ser Cys Ser Lys Glu Ile Gln Met Ala Val Leu Leu Lys Phe Val
130      195          200          205
131 Ser Glu Gly Asp Asn Ile Pro Asp Ala Leu Gly Leu Val Glu Tyr Leu
132      210          215          220
133 Asn Glu Trp Leu Gln Ile Leu Lys Pro Leu Ser Asp Asp Pro Thr Val
134 225          230          235          240
135 Ser Ala Ser Arg Trp Lys Ile Pro Ser Ser Trp Arg Leu Leu Phe Gly
136      245          250          255
137 Ser Gly Leu Pro Pro Ala Leu Phe
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140 <211> LENGTH: 112
141 <212> TYPE: PRT
142 <213> ORGANISM: Homo sapiens

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194 Leu Gln Arg Ala Val His Gly Leu Leu His Tyr Leu Phe His Thr Arg
195          50          55          60
196 Asn His Thr Phe Ile Val Leu His Leu Val Leu Gln Gly Met Val Tyr
197 65          70          75          80
198 Thr Glu Tyr Thr Trp Glu Val Phe Gly Tyr Cys Gln Glu Leu Glu Leu
199          85          90          95
200 Ser Leu His Tyr Leu Leu Leu Pro Tyr Leu Leu Leu Gly Val Asn Leu
201          100          105          110
202 Phe Phe Phe Thr Leu Thr Cys Gly Thr Asn Pro Gly Ile Ile Thr Lys
203          115          120          125
204 Ala Asn Glu Leu Leu Phe Leu His Val Tyr Glu Phe Asp Glu Val Met
205          130          135          140
206 Phe Pro Lys Asn Val Arg Cys Ser Thr Cys Asp Leu Arg Lys Pro Ala
207 145          150          155          160
208 Arg Ser Lys His Cys Ser Val Cys Asn Trp Cys Val His Arg Phe Asp
209          165          170          175
210 His His Cys Val Trp Val Asn Asn Cys Ile Gly Ala Trp Asn Ile Arg
211          180          185          190
212 Tyr Phe Leu Ile Tyr Val Leu Thr Leu Thr Ala Ser Ala Ala Thr Val
213          195          200          205
214 Ala Ile Val Ser Thr Thr Phe Leu Val His Leu Val Val Met Ser Asp
215          210          215          220
216 Leu Tyr Gln Glu Thr Tyr Ile Asp Asp Leu Gly His Leu His Val Met
217 225          230          235          240
218 Asp Thr Val Phe Leu Ile Gln Tyr Leu Phe Leu Thr Phe Pro Arg Ile
219          245          250          255
220 Val Phe Met Leu Gly Phe Val Val Val Leu Ser Phe Leu Leu Gly Gly
221          260          265          270
222 Tyr Leu Leu Phe Val Leu Tyr Leu Ala Ala Thr Asn Gln Thr Thr Asn
223          275          280          285
224 Glu Trp Tyr Arg Gly Asp Trp Ala Trp Cys Gln Arg Cys Pro Leu Val
225          290          295          300
226 Ala Trp Pro Pro Ser Ala Glu Pro Gln Val His Arg Asn Ile His Ser
227 305          310          315          320
228 His Gly Leu Arg Ser Asn Leu Gln Glu Ile Phe Leu Pro Ala Phe Pro
229          325          330          335
230 Cys His Glu Arg Lys Lys Gln Glu
231          340
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233 <211> LENGTH: 97
234 <212> TYPE: PRT
235 <213> ORGANISM: Homo sapiens
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238 1          5          10          15
239 Gly Leu Glu Glu Lys Leu Ser Gln Cys Arg Arg Asp Leu Glu Ala Val
240          20          25          30

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VERIFICATION SUMMARY

DATE: 11/19/2002

PATENT APPLICATION: US/09/743,247A

TIME: 14:43:13

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VERIFICATION SUMMARY

PATENT APPLICATION: **US/09/743,247A**

DATE: 11/19/2002

TIME: 14:43:13

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09/743247

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1/177 534 Rec'd PCT/PTO 05 JAN2001

Sequence listing

<110> Sagami Chemical Research Center; Protegene Inc.

5 <120> Human Proteins Having Hydrophobic Domains And DNAs Encoding These
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Val Ser Lys Leu Ser Pro Glu Glu Val Gln Lys Asn Tyr Glu His Leu
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Tyr Cys Ile Ala Arg Arg Leu Val Asp Asp Thr Asp Ala Met Ser Asn
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10 165 170 175
Tyr Asn Trp Val Arg Leu Gly Thr Phe Pro Thr Pro Ser Pro Gly Ser
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15 Leu Thr Ser Ser Gly Thr Tyr Arg Cys Val Ala Thr Asn Gln Met Gly
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260 265 270
Lys Pro Lys Glu Thr Tyr Gly Gly Ser Asp Leu Arg Glu Asp Ala Ile
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attgaccagc ggtcaactgt gactgtttca gtaatgctac agccctttga ctatgatccg      240
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 Ala Ser Asn Leu Ser Gly Leu Ser Leu Gln Glu Ala Gln Gln Ile Leu
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	Pro Ile Val Phe Ala Arg Ala His Leu Ile Glu Trp Gly Ala Cys Ala	
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Tyr Cys Val	Arg Pro Asn	Ser Gly Ile	Ile Asp Pro	Gly Ser Thr	Val	
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	Gly Thr Ala Ala Ala Pro Ala Lys Pro Ala Pro Pro Ala Thr Pro Gly	
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	Cys Arg Val Leu Ser Gly Leu Gly Leu Met Gly Ala Gly Gly Tyr Val	
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	Tyr Trp Val Ala Arg Lys Pro Met Lys Met Gly Tyr Pro Pro Ser Pro	
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	Asn	Trp	Cys	Val	His	Arg	Phe	Asp	His	His	Cys	Val	Trp	Val	Asn	Asn	
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 5 Val His Leu Val Val Met Ser Asp Leu Tyr Gln Glu Thr Tyr Ile Asp
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 gac ctt gga cac ctc cat gtt atg gac acg gtc ttt ctt att cag tac 1074
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	Val Phe Lys Pro Asn Ser Lys Lys Arg Lys Ile Ser Leu Pro Ile Glu	
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	Asp Tyr Phe Asn Lys Gly Lys Asn Glu Pro Glu Asp Ser Lys Leu Arg	
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	Phe Glu Thr Tyr Gln Leu Ile Trp Gln Gln Met Lys Ser Glu Asn Glu	
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	Gly Gly Gln Ile Lys Leu Arg Glu Ile Pro Thr Ala Ala Leu Val Leu	
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	ggt ata tat gcg tat gtt tgt tca tgc atg cat ctc tgt gta ttt cgt	446
	Gly Ile Tyr Ala Tyr Val Cys Ser Cys Met His Leu Cys Val Phe Arg	
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	Cys Leu Ser Gly Leu Ala Val Glu Val Lys Val Pro Thr Glu Pro Leu	
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	Ser Thr Pro Leu Gly Lys Thr Ala Glu Leu Thr Cys Thr Tyr Ser Thr	
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	Ser Val Gly Asp Ser Phe Ala Leu Glu Trp Ser Phe Val Gln Pro Gly	
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	Lys Pro Ile Ser Glu Ser His Pro Ile Leu Tyr Phe Thr Asn Gly His	
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	ctg tat cca act ggt tct aag tca aag cgg gtc agc ctg ctt cag aac	347
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	Pro Pro Thr Val Gly Val Ala Thr Leu Lys Leu Thr Asp Val His Pro	
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	Tyr Thr Asn Gly Leu Gly Leu Ile Asn Leu Thr Val Leu Val Pro Pro	
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	Ser Asn Pro Leu Cys Ser Gln Ser Gly Gln Thr Ser Val Gly Gly Ser	
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	act gca ctg aga tgc agc tct tcc gag ggg gct cct aag cca gtg tac	587
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	Asn Trp Val Arg Leu Gly Thr Phe Pro Thr Pro Ser Pro Gly Ser Met	
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	acc tcc tgc ggc acc tac cgc tgt gtg gcc acc aac cag atg ggc agt	731
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	Ala Ser Cys Glu Leu Thr Leu Ser Val Thr Glu Pro Ser Gln Gly Arg	
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25	Val Ala Gly Ala Leu Ile Gly Val Leu Leu Gly Val Leu Leu Leu Ser	
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	gtt gct gcg ttc tgc ctg gtc agg ttc cag aaa gag agg ggg aag aag	875
	Val Ala Ala Phe Cys Leu Val Arg Phe Gln Lys Glu Arg Gly Lys Lys	
	260	265 270
30	ccc aag gag aca tat ggg ggt agt gac ctt cgg gag gat gcc atc gct	923
	Pro Lys Glu Thr Tyr Gly Gly Ser Asp Leu Arg Glu Asp Ala Ile Ala	
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	cct ggg atc tct gag cac act tgt atg agg gct gat tct agc aag ggg	971
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	Ser Phe Lys Tyr Glu Asp Phe Gly Pro Leu Phe Thr Ala Lys Phe Phe				
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	Asn Ala Asn Gln Trp Ala Asp Ile Phe Gln Ala Ser Gly Ala Lys Tyr				
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10	Ile Val Leu Thr Ser Lys His His Glu Gly Phe Thr Leu Trp Gly Ser				
	130		135		140
	Glu Tyr Ser Trp Asn Trp Asn Ala Ile Asp Glu Gly Pro Lys Arg Asp				
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	Ile Val Lys Glu Leu Glu Val Ala Ile Arg Asn Arg Thr Asp Leu Arg				
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	Phe Gly Leu Tyr Tyr Ser Leu Phe Glu Trp Phe His Pro Leu Phe Leu				
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	Glu Asp Glu Ser Ser Ser Phe His Lys Arg Gln Phe Pro Val Ser Lys				
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20	Thr Leu Pro Glu Leu Tyr Glu Leu Val Asn Asn Tyr Gln Pro Glu Val				
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	Leu Trp Ser Asp Gly Asp Gly Gly Ala Pro Asp Gln Tyr Trp Asn Ser				
	225		230		235
	Thr Gly Phe Leu Ala Trp Leu Tyr Asn Glu Ser Pro Val Arg Gly Thr				
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	Val Val Thr Asn Asp Arg Trp Gly Ala Gly Ser Ile Cys Lys His Gly				
	260		265		270
	Gly Phe Tyr Thr Cys Ser Asp Arg Tyr Asn Pro Gly His Leu Leu Pro				
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30	His Lys Trp Glu Asn Cys Met Thr Ile Asp Lys Leu Ser Trp Gly Tyr				
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	Arg Arg Glu Ala Gly Ile Ser Asp Tyr Leu Thr Ile Glu Glu Leu Val				
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	Lys Gln Leu Val Glu Thr Val Ser Cys Gly Gly Asn Leu Leu Met Asn				
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 355 360 365
 5 Glu Thr His Thr Trp Arg Ser Gln Asn Asp Thr Val Thr Pro Asp Val
 370 375 380
 Trp Tyr Thr Ser Lys Pro Lys Glu Lys Leu Val Tyr Ala Ile Phe Leu
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 Lys Trp Pro Thr Ser Gly Gln Leu Phe Leu Gly His Pro Lys Ala Ile
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 35 65 70 75 80

35

5

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Thr Phe Leu Arg Gly Ser Gln Thr Gln Ser His Pro Asp Leu Gly Thr

Glu Gly Cys Trp Asp Gln Leu Ser Ala Pro Arg Thr Phe Thr Leu Leu

Asp Pro Lys Ala Ser Leu Leu Thr Lys Ala Phe Leu Asn Gly Ala Leu

15 Asp Gly Val Ile Leu Gly Asp Tyr Leu Ser Arg Thr Pro Glu Pro Arg

Pro Ser Leu Ser His Leu Leu Ser Gln Tyr Tyr Gly Ala Gly Val Ala

Arg Asp Pro Gly Phe Arg Ser Asn Phe Arg Arg Gln Asn Gly Ala Ala

Leu Thr Ser Ala Ser Ile Leu Ala Gln Gln Val Trp Gly Thr Leu Val

Leu Leu Gln Arg Leu Glu Pro Val His Leu Gln Leu Gln Cys Met Ser

25 Gln Glu Gln Leu Ala Gln Val Ala Ala Asn Ala Thr Lys Glu Phe Thr

145 150 155 160

Glu Ala Phe Leu Gly Cys Pro Ala Ile His Pro Arg Cys Arg Trp Gly

Ala Ala Pro Tyr Arg Gly Arg Pro Lys Leu Leu Gln Leu Pro Leu Gly

Phe Leu Tyr Val His His Thr Tyr Val Pro Ala Pro Pro Cys Thr Asp

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	Asn Leu Ser Val Asn Val Glu Asn Gln Ile Lys Ile Lys Val Gln Val		
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	Leu Lys Leu Leu Leu Asn Leu Ser Glu Asn Pro Ala Met Thr Glu Gly		
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	His Val Ala Lys Glu Ile Leu Leu Arg Val Leu Thr Leu Phe Gln Asn		
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	Ile Lys Asn Cys Leu Lys Ile Glu Gly His Leu Ala Val Gln Pro Thr		
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35	Lys Asp Phe Glu Asn Gly Pro Gln Asn Ile Tyr Asn Leu Tyr Glu Gln		

	50	55	60
	Val Ser Tyr Asn Cys Phe Ile Ala Ala Gly Leu Tyr Leu Leu Leu Gly		
	65	70	75
	Gly Phe Ser Phe Cys Gln Val Arg Leu Asn Lys Arg Lys Glu Tyr Met		
5	85	90	95
	Val Arg		
	<210> 39		
	<211> 172		
10	<212> PRT		
	<213> Homo sapiens		
	<400> 39		
	Met Val Gly Pro Ala Pro Arg Arg Arg Leu Arg Pro Leu Ala Ala Leu		
15	1	5	10
	Ala Leu Val Leu Ala Leu Ala Pro Gly Leu Pro Thr Ala Arg Ala Gly		
	20	25	30
	Gln Thr Pro Arg Pro Ala Glu Arg Gly Pro Pro Val Arg Leu Phe Thr		
	35	40	45
20	Glu Glu Glu Leu Ala Arg Tyr Gly Gly Glu Glu Glu Asp Gln Pro Ile		
	50	55	60
	Tyr Leu Ala Val Lys Gly Val Val Phe Asp Val Thr Ser Gly Lys Glu		
	65	70	75
	Phe Tyr Gly Arg Gly Ala Pro Tyr Asn Ala Leu Thr Gly Lys Asp Ser		
25	85	90	95
	Thr Arg Gly Val Ala Lys Met Ser Leu Asp Pro Ala Asp Leu Thr His		
	100	105	110
	Asp Thr Thr Gly Leu Thr Ala Lys Glu Leu Glu Ala Leu Asp Glu Val		
	115	120	125
30	Phe Thr Lys Val Tyr Lys Ala Lys Tyr Pro Ile Val Gly Tyr Thr Ala		
	130	135	140
	Arg Arg Ile Leu Asn Glu Asp Gly Ser Pro Asn Leu Asp Phe Lys Pro		
	145	150	155
	Glu Asp Gln Pro His Phe Asp Ile Lys Asp Glu Phe		
35	165	170	

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<210> 40

<211> 120

<212> PRT

5 <213> Homo sapiens

<400> 40

Met Met Pro Ser Arg Thr Asn Leu Ala Thr Gly Ile Pro Ser Ser Lys

1 5 10 15

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20 25 30

Gln Phe Lys Lys Thr Pro Pro Lys Ile Pro Tyr Lys Ala Ile Ala Leu

35 40 45

Ala Thr Val Leu Phe Leu Ile Gly Ala Phe Leu Ile Ile Ile Gly Ser

15 50 55 60

Leu Leu Leu Ser Gly Tyr Ile Ser Lys Gly Gly Ala Asp Arg Ala Val

65 70 75 80

Pro Val Leu Ile Ile Gly Ile Leu Val Phe Leu Pro Gly Phe Tyr His

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20 Leu Arg Ile Ala Tyr Tyr Ala Ser Lys Gly Tyr Arg Gly Tyr Ser Tyr

100 105 110

Asp Asp Ile Pro Asp Phe Asp Asp

115 120

25 <210> 41

<211> 939

<212> DNA

<213> Homo sapiens

30 <400> 41

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tgaaggaaa tcaaagacga atgtcctagt gcatttgatg gcctgtatct tctccgcaact 180

gagaatggtg ttatctacca gaccttctgt gacatgacct ctgggggtgg cggctggacc 240

35 ctggtggcca gcgtgcatga gaatgacatg cgtgggaagt gcacggtggg cgatcgctgg 300

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	tccagtcagc agggcagcaa agcagactac ccagaggggg acggcaactg ggccaactac	360
	aacacctttg gatctgcaga ggcggccacg agcgatgact acaagaaccc tggctactac	420
	gacatccagg ccaaggacct gggcatctgg cacgtgcccc ataagtcccc catgcagcac	480
	tggagaaaca gctccctgct gaggtaccgc acggacactg gcttctcca gacactggga	540
5	cataatctgt ttggcatcta ccagaaatat ccagtgaat atggagaagg aaagtgttgg	600
	actgacaacg gcccggtgat ccctgtggtc tatgattttg gcgacgcccc gaaaacagca	660
	tcttattact caccctatgg ccagcgggaa ttcactgagg gatttgttca gttcagggtta	720
	tttaataacg agagagcagc caacgccttg tgtgctggaa tgagggtcac cggatgtaac	780
	actgagcacc actgcattgg tggaggagga tactttccag aggccagtcc ccagcagtgt	840
10	ggagattttt ctggttttga ttggagtggg tatggaactc atgttggtta cagcagcagc	900
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<210> 42

<211> 687

15 <212> DNA

<213> Homo sapiens

<400> 42

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	cccgccggcc agaaggagtg cttctaccag cccatgcccc tgaaggcttc gctggagatc	180
	gagtaccaag ttttagatgg agcaggatta gatattgatt tccatcttgc ctctccagaa	240
	ggcaaaacct tagtttttga acaaagaaaa tcagatggag ttcacactgt agagactgaa	300
	gttggtgatt acatgttctg ctttgacaat acattcagca ccatttctga gaagggtgatt	360
25	ttctttgaat taatcctgga taatatggga gaacaggcac aagaacaaga agattggaag	420
	aaatatatta ctggcacaga tatattggat atgaaactgg aagacatcct ggaatccatc	480
	aacagcatca agtccagact aagcaaaagt ggcacatac aaattctgct tagagcattt	540
	gaagctcgtg atcgaaacat acaagaaagc aactttgata gagtcaattt ctggtctatg	600
	gttaatttag tggatcatgt ggtggtgtca gccattcaag tttatatgct gaagagtctg	660
30	tttgaagata agaggaaaag tagaact	687

<210> 43

<211> 1401

<212> DNA

35 <213> Homo sapiens

35 atggataacg tgcagccgaa aataaaacat cgcccccttct gcttcagtggt gaaaggccac 60
gtgaagatgc tgcggctgga tattatcaac tcaactggtaa caacagttatt catgctcatt 120

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	gtatctgtgt tggcactgat accagaaacc acaacattga cagttgggtgg aggggtgttt	180
	gcacttgtga cagcagtatg ctgtcttgcc gacggggccc ttatttaccg gaagcttctg	240
	ttcaatccca gcggtcctta ccagcaaaag cctgtgcatg aaaaaaaga agttttg	297
5	<210> 45	
	<211> 567	
	<212> DNA	
	<213> Homo sapiens	
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	cttccccgac ataccttcgg actagtgcag agcaaaactct tccccctcta ctccacate	180
	tccatgggct gtgccttcat caacctctgc atcttggtt caccagcatgc ttgggctcag	240
15	ctcacattct gggaggccag ccagctttac ctgctgttcc tgagccttac gctggcact	300
	gtcaacgccc gctggctgga accccgcacc acagctgcca tgtgggccct gcaaaccgtg	360
	gagaaggagc gaggcctggg tggggaggta ccaggcagcc accagggtcc cgatccctac	420
	cgccagctgc gagagaagga cccaagtac agtgctctcc gccagaattt cttccgctac	480
	catgggctgt cctctctttg caatctgggc tgcgtcctga gcaatgggct ctgtctcgt	540
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	<210> 46	
	<211> 1089	
	<212> DNA	
25	<213> Homo sapiens	
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	ggttcccaga ccagagcca tccagacctg ggaactgagg gctgctggga ccagctctct	120
30	gccccctgga cttttacgct tttggacccc aaggcatctc tgtaaccaa ggccttctc	180
	aatggcgcgc tggatggggt cactcttgga gactacctga gccggactcc tgagccccgg	240
	ccatccctca gccacttgct gagccagtac tatggggctg ggggtggccag agaccaggg	300
	ttccgcagca acttccgacg gcagaacggt gctgctctga cttcagcctc catcctggcc	360
	cagcaggtgt ggggaaccct tgctcttcta cagaggctgg agccagtaca cctccagctt	420
35	cagtgcata gccaagaaca gctggcccag gtggctgcca atgctaccaa ggaattcact	480

35 <212> DNA

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<213> Homo sapiens

<400> 48

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5	tggggagtga	tcattgtgat	aatgctcgga	atatttttca	atgtccattc	cgctgtgttg	120
	attgaggacg	ttcccttcac	ggagaaagat	tttgagaatg	gccccagaa	catatacaac	180
	ctttacgagc	aagtcagcta	caactgtttc	atcgctgcag	gcctttacct	cctcctcgga	240
	ggcttctctt	tctgccaaag	tcggctcaat	aagcgcaagg	aatacatggt	gcgc	294

10 <210> 49

<211> 516

<212> DNA

<213> Homo sapiens

15 <400> 49

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	gcgctggccc	cggggctgcc	cacagcccgcg	gccgggcaga	caccgcgcgc	tgccgagcgg	120
	gggccccccag	tgcggtttt	caccgaggag	gagctggccc	getatggcgg	ggaggaggaa	180
	gatcagccca	tctacttggc	agtgaaggga	gtggtgtttg	atgtcacctc	cggaaaggag	240
20	ttttatggac	gaggagcccc	ctacaatgcc	ttgacgggga	aggactccac	tagaggggta	300
	gccaaagatgt	cottggatcc	tgcagacctc	acccatgaca	ctacgggtct	caaggccaaag	360
	gaactggagg	ccctggatga	ggtcttcacc	aaagtgtaca	aagccaaata	ccccatcgte	420
	ggctacactg	cccggagaat	tctcaatgag	gatggcagcc	ctaacctgga	cttcaagcct	480
	gaagaccagc	cccattttga	catcaaggat	gagttc			516

25

<210> 50

<211> 360

<212> DNA

<213> Homo sapiens

30

<400> 50

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	aggtctcca	gcacagacga	tggctacatt	gaccttcagt	ttaagaaaac	ccctcctaag	120
	atcccttata	aggccatcgc	acttgccact	gtgctgtttt	tgattggcgc	ctttctcatt	180
35	attataggct	ccctcctgct	gtcaggctac	atcagcaaag	ggggggcaga	ccgggcccgtt	240

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ccagtgtga tcattggcat tetggtgttc ctaccggat tttaccacct ggcacatgct 300
tactatgcat ccaaaggcta ccgtgggttac tcctatgatg acattccaga ctttgatgac 360

<210> 51

5 <211> 1065

<212> DNA

<213> Homo sapiens

<220>

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10 <222> (2)...(943)

<400> 51

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Met Asn Gln Leu Ser Phe Leu Leu Phe Leu Ile Ala Thr Thr Arg Gly

15 1 5 10 15

tgg agt aca gat gag gct aat act tac ttc aag gaa tgg acc tgt tct 97

Trp Ser Thr Asp Glu Ala Asn Thr Tyr Phe Lys Glu Trp Thr Cys Ser

20 25 30

tcg tct cca tct ctg ccc aga agc tgc aag gaa atc aaa gac gaa tgt 145

20 Ser Ser Pro Ser Leu Pro Arg Ser Cys Lys Glu Ile Lys Asp Glu Cys

35 40 45

cct agt gca ttt gat ggc ctg tat ttt ctc cgc act gag aat ggt gtt 193

Pro Ser Ala Phe Asp Gly Leu Tyr Phe Leu Arg Thr Glu Asn Gly Val

50 55 60

25 atc tac cag acc ttc tgt gac atg acc tct ggg ggt ggc ggc tgg acc 241

Ile Tyr Gln Thr Phe Cys Asp Met Thr Ser Gly Gly Gly Gly Trp Thr

65 70 75 80

ctg gtg gcc agc gtg cat gag aat gac atg cgt ggg aag tgc acg gtg 289

Leu Val Ala Ser Val His Glu Asn Asp Met Arg Gly Lys Cys Thr Val

30 85 90 95

ggc gat cgc tgg tcc agt cag cag ggc agc aaa gca gac tac cca gag 337

Gly Asp Arg Trp Ser Ser Gln Gln Gly Ser Lys Ala Asp Tyr Pro Glu

100 105 110

ggg gac ggc aac tgg gcc aac tac aac acc ttt gga tct gca gag gcg 385

35 Gly Asp Gly Asn Trp Ala Asn Tyr Asn Thr Phe Gly Ser Ala Glu Ala

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	115	120	125	
	gcc acg agc gat gac tac aag aac cct ggc tac tac gac atc cag gcc			433
	Ala Thr Ser Asp Asp Tyr Lys Asn Pro Gly Tyr Tyr Asp Ile Gln Ala			
	130	135	140	
5	aag gac ctg ggc atc tgg cac gtg ccc aat aag tcc ccc atg cag cac			481
	Lys Asp Leu Gly Ile Trp His Val Pro Asn Lys Ser Pro Met Gln His			
	145	150	155	160
	tgg aga aac agc tcc ctg ctg agg tac cgc acg gac act ggc ttc ctc			529
	Trp Arg Asn Ser Ser Leu Leu Arg Tyr Arg Thr Asp Thr Gly Phe Leu			
10	165	170	175	
	cag aca ctg gga cat aat ctg ttt ggc atc tac cag aaa tat cca gtg			577
	Gln Thr Leu Gly His Asn Leu Phe Gly Ile Tyr Gln Lys Tyr Pro Val			
	180	185	190	
	aaa tat gga gaa gga aag tgt tgg act gac aac ggc ccg gtg atc cct			625
15	Lys Tyr Gly Glu Gly Lys Cys Trp Thr Asp Asn Gly Pro Val Ile Pro			
	195	200	205	
	gtg gtc tat gat ttt ggc gac gcc cag aaa aca gca tct tat tac tca			673
	Val Val Tyr Asp Phe Gly Asp Ala Gln Lys Thr Ala Ser Tyr Tyr Ser			
	210	215	220	
20	ccc tat ggc cag cgg gaa ttc act gcg gga ttt gtt cag ttc agg gta			721
	Pro Tyr Gly Gln Arg Glu Phe Thr Ala Gly Phe Val Gln Phe Arg Val			
	225	230	235	240
	ttt aat aac gag aga gca gcc aac gcc ttg tgt gct gga atg agg gtc			769
	Phe Asn Asn Glu Arg Ala Ala Asn Ala Leu Cys Ala Gly Met Arg Val			
25	245	250	255	
	acc gga tgt aac act gag cac cac tgc att ggt gga gga gga tac ttt			817
	Thr Gly Cys Asn Thr Glu His His Cys Ile Gly Gly Gly Tyr Phe			
	260	265	270	
	cca gag gcc agt ccc cag cag tgt gga gat ttt tct ggt ttt gat tgg			865
30	Pro Glu Ala Ser Pro Gln Gln Cys Gly Asp Phe Ser Gly Phe Asp Trp			
	275	280	285	
	agt gga tat gga act cat gtt ggt tac agc agc agc cgt gag ata act			913
	Ser Gly Tyr Gly Thr His Val Gly Tyr Ser Ser Ser Arg Glu Ile Thr			
	290	295	300	
35	gag gca gct gtg ctt cta ttc tat cgt tgagagtttt gtgggaggga			960

95

	agcgcctcccg aggcgcgcggg agcctgcagagaggacagcc ggccctgcgcc gggac	55
5	atg cgg ccc cag gag ctc ccc agg ctc gcg ttc ccg ttg ctg ctg ttg Met Arg Pro Gln Glu Leu Pro Arg Leu Ala Phe Pro Leu Leu Leu Leu	103
	1 5 10 15	
	ctg ttg ctg ctg ctg ccg ccg ccg ccg tgc cct gcc cac agc gcc acg Leu Leu Leu Leu Leu Pro Pro Pro Pro Cys Pro Ala His Ser Ala Thr	151
10	20 25 30	
	cgc ttc gac ccc acc tgg gag tcc ctg gac gcc cgc cag ctg ccc gcg Arg Phe Asp Pro Thr Trp Glu Ser Leu Asp Ala Arg Gln Leu Pro Ala	199
	35 40 45	
	tgg ttt gac cag gcc aag ttc ggc atc ttc atc cac tgg gga gtg ttt Trp Phe Asp Gln Ala Lys Phe Gly Ile Phe Ile His Trp Gly Val Phe	247
15	50 55 60	
	tcc gtg ccc agc ttc ggt agc gag tgg ttc tgg tgg tat tgg caa aag Ser Val Pro Ser Phe Gly Ser Glu Trp Phe Trp Trp Tyr Trp Gln Lys	295
	65 70 75 80	
20	gaa aag ata ccg aag tat gtg gaa ttt atg aaa gat aat tac cct cct Glu Lys Ile Pro Lys Tyr Val Glu Phe Met Lys Asp Asn Tyr Pro Pro	343
	85 90 95	
	agt ttc aaa tat gaa gat ttt gga cca cta ttt aca gca aaa ttt ttt Ser Phe Lys Tyr Glu Asp Phe Gly Pro Leu Phe Thr Ala Lys Phe Phe	391
25	100 105 110	
	aat gcc aac cag tgg gca gat att ttt cag gcc tct ggt gcc aaa tac Asn Ala Asn Gln Trp Ala Asp Ile Phe Gln Ala Ser Gly Ala Lys Tyr	439
	115 120 125	
	att gtc tta act tcc aaa cat cat gaa ggc ttt acc ttg tgg ggg tca Ile Val Leu Thr Ser Lys His His Glu Gly Phe Thr Leu Trp Gly Ser	487
30	130 135 140	
	gaa tat tcg tgg aac tgg aat gcc ata gat gag ggg ccc aag agg gac Glu Tyr Ser Trp Asn Trp Asn Ala Ile Asp Glu Gly Pro Lys Arg Asp	535
	145 150 155 160	
35	att gtc aag gaa ctt gag gta gcc att agg aac aga act gac ctg cgt	583

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Ile Val Lys Glu Leu Glu Val Ala Ile Arg Asn Arg Thr Asp Leu Arg
 165 170 175
 ttt gga ctg tac tat tcc ctt ttt gaa tgg ttt cat ccg ctc ttc ctt 631
 Phe Gly Leu Tyr Tyr Ser Leu Phe Glu Trp Phe His Pro Leu Phe Leu
 5 180 185 190
 gag gat gaa tcc agt tca ttc cat aag cgg caa ttt cca gtt tct aag 679
 Glu Asp Glu Ser Ser Ser Phe His Lys Arg Gln Phe Pro Val Ser Lys
 195 200 205
 aca ttg cca gag ctc tat gag tta gtg aac aac tat cag cct gag gtt 727
 10 Thr Leu Pro Glu Leu Tyr Glu Leu Val Asn Asn Tyr Gln Pro Glu Val
 210 215 220
 ctg tgg tgg gat ggt gac gga gga gca ccg gat caa tac tgg aac agc 775
 Leu Trp Ser Asp Gly Asp Gly Gly Ala Pro Asp Gln Tyr Trp Asn Ser
 225 230 235 240
 15 aca ggc ttc ttg gcc tgg tta tat aat gaa agc cca gtt cgg ggc aca 823
 Thr Gly Phe Leu Ala Trp Leu Tyr Asn Glu Ser Pro Val Arg Gly Thr
 245 250 255
 gta gtc acc aat gat cgt tgg gga gct ggt agc atc tgt aag cat ggt 871
 Val Val Thr Asn Asp Arg Trp Gly Ala Gly Ser Ile Cys Lys His Gly
 20 260 265 270
 ggc ttc tat acc tgc agt gat cgt tat aac cca gga cat ctt ttg cca 919
 Gly Phe Tyr Thr Cys Ser Asp Arg Tyr Asn Pro Gly His Leu Leu Pro
 275 280 285
 cat aaa tgg gaa aac tgc atg aca ata gac aaa ctg tcc tgg ggc tat 967
 25 His Lys Trp Glu Asn Cys Met Thr Ile Asp Lys Leu Ser Trp Gly Tyr
 290 295 300
 agg agg gaa gct gga atc tct gac tat ctt aca att gaa gaa ttg gtg 1015
 Arg Arg Glu Ala Gly Ile Ser Asp Tyr Leu Thr Ile Glu Glu Leu Val
 305 310 315 320
 30 aag caa ctt gta gag aca gtt tca tgt gga gga aat ctt ttg atg aat 1063
 Lys Gln Leu Val Glu Thr Val Ser Cys Gly Gly Asn Leu Leu Met Asn
 325 330 335
 att ggg ccc aca cta gat ggc acc att tct gta gtt ttt gag gag cga 1111
 Ile Gly Pro Thr Leu Asp Gly Thr Ile Ser Val Val Phe Glu Glu Arg
 35 340 345 350

[illegible]

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	Leu Arg Gln Met Gly Ser Trp Leu Lys Val Asn Gly Glu Ala Ile Tyr	
	355 360 365	
5	gaa acc cat acc tgg cga tcc cag aat gac act gtc acc cca gat gtg	1207
	Glu Thr His Thr Trp Arg Ser Gln Asn Asp Thr Val Thr Pro Asp Val	
	370 375 380	
	tgg tac aca tcc aag cct aaa gaa aaa tta gtc tat gcc att ttt ctt	1255
	Trp Tyr Thr Ser Lys Pro Lys Glu Lys Leu Val Tyr Ala Ile Phe Leu	
	385 390 395 400	
10	aaa tgg ccc aca tca gga cag ctg ttc ctt ggc cat ccc aaa gct att	1303
	Lys Trp Pro Thr Ser Gly Gln Leu Phe Leu Gly His Pro Lys Ala Ile	
	405 410 415	
	ctg ggg gca aca gag gtg aaa cta ctg ggc cat gga cag cca ctt aac	1351
	Leu Gly Ala Thr Glu Val Lys Leu Leu Gly His Gly Gln Pro Leu Asn	
15	420 425 430	
	tgg att tct ttg gag caa aat ggc att atg gta gaa ctg cca cag cta	1399
	Trp Ile Ser Leu Glu Gln Asn Gly Ile Met Val Glu Leu Pro Gln Leu	
	435 440 445	
20	acc att cat cag atg ccg tgt aaa tgg ggc tgg gct cta gcc ctg act	1447
	Thr Ile His Gln Met Pro Cys Lys Trp Gly Trp Ala Leu Ala Leu Thr	
	450 455 460	
	aat gtg atc taaagtgcag cagagtggct gatgctgcaa gttatgtcta aggc	1500
	Asn Val Ile	
	465	
25	taggaactat caggtgtcta taattgtagc acatggagaa agcaaagtga aaactggata	1560
	agaaaattat ttggcagtt cagcccttcc cctttttccc actaaatttt ttcttaaatt	1620
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35	<222> (114)...(413)	

<221> CDS

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<222> (272)...(841)

<400> 55

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	gggtgctgcg gattgaggtc ccggttccta acgaatctct gctggattgg ccgtaaccct	180
	gtcccgagc gggctcacag ggtctgaagg ccacgcatga ggcaaaggta aagttctgag	240
	ccaccgggtg cctccttccc aggactgcaa g atg gag gaa ggc ggg aac cta	292
	Met Glu Glu Gly Gly Asn Leu	
10	1 5	
	gga ggc ctg att aag atg gtc cat cta ctg gtc ttg tca ggt gcc tgg	340
	Gly Gly Leu Ile Lys Met Val His Leu Leu Val Leu Ser Gly Ala Trp	
	10 15 20	
	ggc atg caa atg tgg gtg acc ttc gtc tca ggc ttc ctg ctt ttc cga	388
15	Gly Met Gln Met Trp Val Thr Phe Val Ser Gly Phe Leu Leu Phe Arg	
	25 30 35	
	agc ctt ccc cga cat acc ttc gga cta gtg cag agc aaa ctc ttc ccc	436
	Ser Leu Pro Arg His Thr Phe Gly Leu Val Gln Ser Lys Leu Phe Pro	
	40 45 50 55	
20	ttc tac ttc cac atc tcc atg ggc tgt gcc ttc atc aac ctc tgc atc	484
	Phe Tyr Phe His Ile Ser Met Gly Cys Ala Phe Ile Asn Leu Cys Ile	
	60 65 70	
	ttg gct tca cag cat gct tgg gct cag ctc aca ttc tgg gag gcc agc	532
	Leu Ala Ser Gln His Ala Trp Ala Gln Leu Thr Phe Trp Glu Ala Ser	
25	75 80 85	
	cag ctt tac ctg ctg ttc ctg agc ctt acg ctg gcc act gtc aac gcc	580
	Gln Leu Tyr Leu Leu Phe Leu Ser Leu Thr Leu Ala Thr Val Asn Ala	
	90 95 100	
	cgc tgg ctg gaa ccc cgc acc aca gct gcc atg tgg gcc ctg caa acc	628
30	Arg Trp Leu Glu Pro Arg Thr Thr Ala Ala Met Trp Ala Leu Gln Thr	
	105 110 115	
	gtg gag aag gag cga ggc ctg ggt ggg gag gta cca ggc agc cac cag	676
	Val Glu Lys Glu Arg Gly Leu Gly Gly Glu Val Pro Gly Ser His Gln	
	120 125 130 135	
35	ggg ccc gat ccc tac cgc cag ctg cga gag aag gac ccc aag tac agt	724

	Gly Pro Asp Pro Tyr Arg Gln Leu Arg Glu Lys Asp Pro Lys Tyr Ser	
	140 145 150	
	gct ctc cgc cag aat ttc ttc cgc tac cat ggg ctg tcc tct ctt tgc	772
	Ala Leu Arg Gln Asn Phe Phe Arg Tyr His Gly Leu Ser Ser Leu Cys	
5	155 160 165	
	aat ctg ggc tgc gtc ctg agc aat ggg ctc tgt ctc gct ggc ctt gcc	820
	Asn Leu Gly Cys Val Leu Ser Asn Gly Leu Cys Leu Ala Gly Leu Ala	
	170 175 180	
	ctg gaa ata agg agc ctc tagcatgggc cctgcatgct aataaatgct tcttcag	875
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	atattggagc caacactcca gatgctacaa aaggctgtcc agatgtccaa gcttccttgc	120
	cagatgccaa agccaagtcc ccaccgacc atg gtg gac agc ctc ctg gca gtc	173
25	Met Val Asp Ser Leu Leu Ala Val	
	1 5	
	acc ctg gct gga aac ctg ggc ctg acc ttc ctc cga ggt tcc cag acc	221
	Thr Leu Ala Gly Asn Leu Gly Leu Thr Phe Leu Arg Gly Ser Gln Thr	
	10 15 20	
30	cag agc cat cca gac ctg gga act gag ggc tgc tgg gac cag ctc tct	269
	Gln Ser His Pro Asp Leu Gly Thr Glu Gly Cys Trp Asp Gln Leu Ser	
	25 30 35 40	
	gcc cct cgg acc ttt acg ctt ttg gac ccc aag gca tct ctg tta acc	317
	Ala Pro Arg Thr Phe Thr Leu Leu Asp Pro Lys Ala Ser Leu Leu Thr	
35	45 50 55	

	aag gcc ttc ctc aat ggc gcc ctg gat ggg gtc atc ctt gga gac tac	365
	Lys Ala Phe Leu Asn Gly Ala Leu Asp Gly Val Ile Leu Gly Asp Tyr	
	60 65 70	
	ctg agc cgg act cct gag ccc cgg cca tcc ctc agc cac ttg ctg agc	413
5	Leu Ser Arg Thr Pro Glu Pro Arg Pro Ser Leu Ser His Leu Leu Ser	
	75 80 85	
	cag tac tat ggg gct ggg gtg gcc aga gac cca ggg ttc cgc agc aac	461
	Gln Tyr Tyr Gly Ala Gly Val Ala Arg Asp Pro Gly Phe Arg Ser Asn	
	90 95 100	
10	ttc cga cgg cag aac ggt gct gct ctg act tca gcc tcc atc ctg gcc	509
	Phe Arg Arg Gln Asn Gly Ala Ala Leu Thr Ser Ala Ser Ile Leu Ala	
	105 110 115 120	
	cag cag gtg tgg gga acc ctt gtc ctt cta cag agg ctg gag cca gta	557
	Gln Gln Val Trp Gly Thr Leu Val Leu Leu Gln Arg Leu Glu Pro Val	
15	125 130 135	
	cac ctc cag ctt cag tgc atg agc caa gaa cag ctg gcc cag gtg gct	605
	His Leu Gln Leu Gln Cys Met Ser Gln Glu Gln Leu Ala Gln Val Ala	
	140 145 150	
	gcc aat gct acc aag gaa ttc act gag gcc ttc ctg gga tgc ccg gcc	653
20	Ala Asn Ala Thr Lys Glu Phe Thr Glu Ala Phe Leu Gly Cys Pro Ala	
	155 160 165	
	atc cac ccc cgc tgc cgc tgg gga gcg gcg cct tat cgg ggc cgc ccg	701
	Ile His Pro Arg Cys Arg Trp Gly Ala Ala Pro Tyr Arg Gly Arg Pro	
	170 175 180	
25	aag ctg ctg cag ctg ccg ctg gga ttc ttg tac gtg cat cac acc tac	749
	Lys Leu Leu Gln Leu Pro Leu Gly Phe Leu Tyr Val His His Thr Tyr	
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	gtg cct gca cca ccc tgc acg gac ttc acg cgc tgc gca gcc aac atg	797
	Val Pro Ala Pro Pro Cys Thr Asp Phe Thr Arg Cys Ala Ala Asn Met	
30	205 210 215	
	cgc tcc atg cag cgc tac cac cag gac acg caa ggc tgg gga gac atc	845
	Arg Ser Met Gln Arg Tyr His Gln Asp Thr Gln Gly Trp Gly Asp Ile	
	220 225 230	
	ggc tac agt ttc gtg gtg ggc tcg gac ggc tac gtg tac gag gga cgc	893
35	Gly Tyr Ser Phe Val Val Gly Ser Asp Gly Tyr Val Tyr Glu Gly Arg	

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	gctggagacc tccgcgtgg ccccgcgag cctcctgcc tggcccgcg ctgcggtct	120
	gccgcggcgg cagc atg ggt ggc ccc cgg ggc gcg ggc tgg gtg gcg gcg	170
	Met Gly Gly Pro Arg Gly Ala Gly Trp Val Ala Ala	
	1 5 10	
5	ggc ctg ctg ctc ggc gcg ggc gcc tgc tac tgc att tac agg ctg acc	218
	Gly Leu Leu Leu Gly Ala Gly Ala Cys Tyr Cys Ile Tyr Arg Leu Thr	
	15 20 25	
	cgg ggt cgg cgg cgg ggc gac cgc gag ctc ggg ata cgc tct tcg aag	266
	Arg Gly Arg Arg Arg Gly Asp Arg Glu Leu Gly Ile Arg Ser Ser Lys	
10	30 35 40	
	tcc gca gaa gac tta act gat ggt tca tat gat gat gtt cta aat gct	314
	Ser Ala Glu Asp Leu Thr Asp Gly Ser Tyr Asp Asp Val Leu Asn Ala	
	45 50 55 60	
	gaa caa ctt cag aaa ctc ctt tac ctg ctg gag tca acg gag gat cct	362
15	Glu Gln Leu Gln Lys Leu Leu Tyr Leu Leu Glu Ser Thr Glu Asp Pro	
	65 70 75	
	gta att att gaa aga gct ttg att act ttg ggt aac aat gca gcc ttt	410
	Val Ile Ile Glu Arg Ala Leu Ile Thr Leu Gly Asn Asn Ala Ala Phe	
	80 85 90	
20	tca gtt aac caa gct att att cgt gaa ttg ggt ggt att cca att gtt	458
	Ser Val Asn Gln Ala Ile Ile Arg Glu Leu Gly Gly Ile Pro Ile Val	
	95 100 105	
	gca aac aaa atc aac cat tcc aac cag agt att aaa gag aaa gct tta	506
	Ala Asn Lys Ile Asn His Ser Asn Gln Ser Ile Lys Glu Lys Ala Leu	
25	110 115 120	
	aat gca cta aat aac ctg agt gtg aat gtt gaa aat caa atc aag ata	554
	Asn Ala Leu Asn Asn Leu Ser Val Asn Val Glu Asn Gln Ile Lys Ile	
	125 130 135 140	
	aag gtg caa gtt ttg aaa ctg ctt ttg aat ttg tct gaa aat cca gcc	602
30	Lys Val Gln Val Leu Lys Leu Leu Leu Asn Leu Ser Glu Asn Pro Ala	
	145 150 155	
	atg aca gaa gga ctt ctc cgt gcc caa gtg gat tca tca ttc ctt tcc	650
	Met Thr Glu Gly Leu Leu Arg Ala Gln Val Asp Ser Ser Phe Leu Ser	
	160 165 170	
35	ctt tat gac agc cac gta gca aag gag att ctt ctt cga gta ctt acg	698

Leu Tyr Asp Ser His Val Ala Lys Glu Ile Leu Leu Arg Val Leu Thr	
175 180 185	
cta ttt cag aat ata aag aac tgc ctc aaa ata gaa ggc cat tta gct	746
Leu Phe Gln Asn Ile Lys Asn Cys Leu Lys Ile Glu Gly His Leu Ala	
190 195 200	
gtg cag cct act ttc act gaa ggt tca ttg ttt ttc ctg tta cat gga	794
Val Gln Pro Thr Phe Thr Glu Gly Ser Leu Phe Phe Leu Leu His Gly	
205 210 215 220	
gaa gaa tgt gcc cag aaa ata aga gct tta gtt gat cac cat gat gca	842
Glu Glu Cys Ala Gln Lys Ile Arg Ala Leu Val Asp His His Asp Ala	
225 230 235	
gag gtg aag gaa aag gtt gta aca ata ata ccc aaa atc tga	884
Glu Val Lys Glu Lys Val Val Thr Ile Ile Pro Lys Ile	
240 245	
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ctc ctg tgc tgt ggg ccg aag ctg gcc gcc tgc ggc atc gtc ctc agc	104
Leu Leu Cys Cys Gly Pro Lys Leu Ala Ala Cys Gly Ile Val Leu Ser	
5 10 15	
gcc tgg gga gtg atc atg ttg ata atg ctc gga ata ttt ttc aat gtc	152
Ala Trp Gly Val Ile Met Leu Ile Met Leu Gly Ile Phe Phe Asn Val	
20 25 30 35	
cat tcc gct gtg ttg att gag gac gtt ccc ttc acg gag aaa gat ttt	200
His Ser Ala Val Leu Ile Glu Asp Val Pro Phe Thr Glu Lys Asp Phe	

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	40	45	50	
	gag aat ggc ccc cag aac ata tac aac ctt tac gag caa gtc agc tac			248
	Glu Asn Gly Pro Gln Asn Ile Tyr Asn Leu Tyr Glu Gln Val Ser Tyr			
	55	60	65	
5	aac tgt ttc atc gct gca ggc ctt tac ctc ctc ctc gga ggc ttc tot			296
	Asn Cys Phe Ile Ala Ala Gly Leu Tyr Leu Leu Leu Gly Gly Phe Ser			
	70	75	80	
	ttc tgc caa gtt cgg ctc aat aag cgc aag gaa tac atg gtg cgc			341
	Phe Cys Gln Val Arg Leu Asn Lys Arg Lys Glu Tyr Met Val Arg			
10	85	90	95	
	tagggcccc ggcgcgttcc cccgcctccag cccctcctct atttaaagac tccctgcacc			400
	gtgtcaccga ggctgcgtcc cacccttgcc ggcgcctct gtgggactgg gtttcccggg			460
	cgagagactg aatcccttct cccatctctg gcacccggcc cccgtggaga gggtgaggg			520
	tggggggctg ttccgtctct ccacccttcg ctgtgtcccg tatctcaata aagagaatct			580
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	Met Val Gly Pro Ala Pro Arg Arg Arg			
	1	5		
	ctg cgg ccg ctg gca gcg ctg gcc ctg gtc ctg gcg ctg gcc ccg ggg			99
30	Leu Arg Pro Leu Ala Ala Leu Ala Leu Val Leu Ala Leu Ala Pro Gly			
	10	15	20	25
	ctg ccc aca gcc cgg gcc ggg cag aca ccg cgc cct gcc gag cgg ggg			147
	Leu Pro Thr Ala Arg Ala Gly Gln Thr Pro Arg Pro Ala Glu Arg Gly			
	30	35	40	
35	ccc cca gtg cgg ctt ttc acc gag gag gag ctg gcc cgc tat gcc ggg			195

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ttcttattat taagtagttt attttaaaaa tatctgagta tattatcctg tacacttate 920
 cctaccttca tgttccagtg gaagacctta gtaaatcaa agatcagtga gttcatctgt 980
 aatatttttt ttacttgctt tcttactgac agcaaccagg aattttttta tctgcagag 1040
 caagttttca aaatgtaaact acttcctctg tttaacagtc cttggaccat tctgatccag 1100
 5 ttcaccagta ggttggacag catataattt gcatcatttt gtcccttgta aatcaagatg 1160
 ttctgcagat tattccttta acggccggac ttttggtctg ttctaatga aacatgtagt 1220
 ggttattatt tagagtttat agccgtattg ctagcacctt gtagtatgtc atcattctgc 1280
 tcatgattcc aaggatcagc ctggatgcct agaggactag atcaccttag tttgatteta 1340
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 10 cctagaaata aaatgagta acttc 1425

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<211> 307

<212> PRT

15 <213> Homo sapiens

<400> 61

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 20 25 30
 Cys Arg Lys Tyr Phe Lys Met Leu Ser Arg Lys Leu Ala Gln Leu Pro
 35 40 45
 Asp Arg Cys Thr Leu Lys Thr Gly His Tyr Asn Ile Asn Phe Ile Ser
 25 50 55 60
 Ser Leu Gly Val Ser Tyr Met Met Leu Cys Thr Glu Asn Tyr Pro Asn
 65 70 75 80
 Val Leu Ala Phe Ser Phe Leu Asp Glu Leu Gln Lys Glu Phe Ile Thr
 85 90 95
 30 Thr Tyr Asn Met Met Lys Thr Asn Thr Ala Val Arg Pro Tyr Cys Phe
 100 105 110
 Ile Glu Phe Asp Asn Phe Ile Gln Arg Thr Lys Gln Arg Tyr Asn Asn
 115 120 125
 Pro Arg Ser Leu Ser Thr Lys Ile Asn Leu Ser Asp Met Gln Thr Glu
 35 130 135 140

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Ile Lys Leu Arg Pro Pro Tyr Gln Ile Ser Met Cys Glu Leu Gly Ser
 145 150 155 160
 Ala Asn Gly Val Thr Ser Ala Phe Ser Val Asp Cys Lys Gly Ala Gly
 165 170 175
 5 Lys Ile Ser Ser Ala His Gln Arg Leu Glu Pro Ala Thr Leu Ser Gly
 180 185 190
 Ile Val Gly Phe Ile Leu Ser Leu Leu Cys Gly Ala Leu Asn Leu Ile
 195 200 205
 Arg Gly Phe His Ala Ile Glu Ser Leu Leu Gln Ser Asp Gly Asp Asp
 10 210 215 220
 Phe Asn Tyr Ile Ile Ala Phe Phe Leu Gly Thr Ala Ala Cys Leu Tyr
 225 230 235 240
 Gln Cys Tyr Leu Leu Val Tyr Tyr Thr Gly Trp Arg Asn Val Lys Ser
 245 250 255
 15 Phe Leu Thr Phe Gly Leu Ile Cys Leu Cys Asn Met Tyr Leu Tyr Glu
 260 265 270
 Leu Arg Asn Leu Trp Gln Leu Phe Phe His Val Thr Val Gly Ala Phe
 275 280 285
 Val Thr Leu Gln Ile Trp Leu Arg Gln Ala Gln Gly Lys Ala Pro Asp
 20 290 295 300
 Tyr Asp Val
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 <210> 62
 25 <211> 183
 <212> PRT
 <213> Homo sapiens

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 Trp Ala Ile Glu Leu Ser Gly Pro Gly Gly Gly Ser Arg Gly Arg Ser
 20 25 30
 Asp Arg Gly Ser Gly Gln Gly Asp Ser Leu Tyr Pro Val Gly Tyr Leu
 35 35 40 45

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Pro Ser Asn Val Asn Leu Thr Cys Gln Phe Thr Thr Ser Gly Asp Leu
 85 90 95
 Asn Ala Val Asn Val Thr Trp Lys Lys Asp Gly Glu Gln Leu Glu Asn
 100 105 110
 5 Asn Tyr Leu Val Ser Ala Thr Gly Ser Thr Leu Tyr Thr Gln Tyr Arg
 115 120 125
 Phe Thr Ile Ile Asn Ser Lys Gln Met Gly Ser Tyr Ser Cys Phe Phe
 130 135 140
 Arg Glu Glu Lys Glu Gln Arg Gly Thr Phe Asn Phe Lys Val Pro Glu
 10 145 150 155 160
 Leu His Gly Lys Asn Lys Pro Leu Ile Ser Tyr Val Gly Asp Ser Thr
 165 170 175
 Val Leu Thr Cys Lys Cys Gln Asn Cys Phe Pro Leu Asn Trp Thr Trp
 180 185 190
 15 Tyr Ser Ser Asn Gly Ser Val Lys Val Pro Val Gly Val Gln Met Asn
 195 200 205
 Lys Tyr Val Ile Asn Gly Thr Tyr Ala Asn Glu Thr Lys Leu Lys Ile
 210 215 220
 Thr Gln Leu Leu Glu Glu Asp Gly Glu Ser Tyr Trp Cys Arg Ala Leu
 20 225 230 235 240
 Phe Gln Leu Gly Glu Ser Glu Glu His Ile Glu Leu Val Val Leu Ser
 245 250 255
 Tyr Leu Val Pro Leu Lys Pro Phe Leu Val Ile Val Ala Glu Val Ile
 260 265 270
 25 Leu Leu Val Ala Thr Ile Leu Leu Cys Glu Lys Tyr Thr Gln Lys Lys
 275 280 285
 Lys Lys His Ser Asp Glu Gly Lys Glu Phe Glu Gln Ile Glu Gln Leu
 290 295 300
 Lys Ser Asp Asp Ser Asn Gly Ile Glu Asn Asn Val Pro Arg His Arg
 30 305 310 315 320
 Lys Asn Glu Ser Leu Gly Gln
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<210> 64

35 <211> 223

35 <211> 48

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				20						25					30	
	Ala	Glu	Gly	Cys	Gly	Gly	Ser	Lys	Glu	His	Ser	Phe	Gln	His	Pro	Phe
				35					40					45		
	Leu	Gln	Ala	Val	Gly	Met	Phe	Leu	Gly	Glu	Phe	Ser	Cys	Leu	Ala	Ala
25				50				55						60		
	Phe	Tyr	Leu	Leu	Arg	Cys	Arg	Ala	Ala	Gly	Gln	Ser	Asp	Ser	Ser	Val
	65					70					75					80
	Asp	Pro	Gln	Gln	Pro	Phe	Asn	Pro	Leu	Leu	Phe	Leu	Pro	Pro	Ala	Leu
					85						90					95
30	Cys	Asp	Met	Thr	Gly	Thr	Ser	Leu	Met	Tyr	Val	Ala	Leu	Asn	Met	Thr
					100					105					110	
	Ser	Ala	Ser	Ser	Phe	Gln	Met	Leu	Arg	Gly	Ala	Val	Ile	Ile	Phe	Thr
					115					120					125	
	Gly	Leu	Phe	Ser	Val	Ala	Phe	Leu	Gly	Arg	Arg	Leu	Val	Leu	Ser	Gln
35					130					135						140

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Trp Leu Gly Ile Leu Ala Thr Ile Ala Gly Leu Val Val Val Gly Leu
 145 150 155 160
 Ala Asp Leu Leu Ser Lys His Asp Ser Gln His Lys Leu Ser Glu Val
 165 170 175
 5 Ile Thr Gly Asp Leu Leu Ile Ile Met Ala Gln Ile Ile Val Ala Ile
 180 185 190
 Gln Met Val Leu Glu Glu Lys Phe Val Tyr Lys His Asn Val His Pro
 195 200 205
 Leu Arg Ala Val Gly Thr Glu Gly Leu Phe Gly Phe Val Ile Leu Ser
 10 210 215 220
 Leu Leu Leu Val Pro Met Tyr Tyr Ile Pro Ala Gly Ser Phe Ser Gly
 225 230 235 240
 Asn Pro Arg Gly Thr Leu Glu Asp Ala Leu Asp Ala Phe Cys Gln Val
 245 250 255
 15 Gly Gln Gln Pro Leu Ile Ala Val Ala Leu Leu Gly Asn Ile Ser Ser
 260 265 270
 Ile Ala Phe Phe Asn Phe Ala Gly Ile Ser Val Thr Lys Glu Leu Ser
 275 280 285
 Ala Thr Thr Arg Met Val Leu Asp Ser Leu Arg Thr Val Val Ile Trp
 20 290 295 300
 Ala Leu Ser Leu Ala Leu Gly Trp Glu Ala Phe His Ala Leu Gln Ile
 305 310 315 320
 Leu Gly Phe Leu Ile Leu Leu Ile Gly Thr Ala Leu Tyr Asn Gly Leu
 325 330 335
 25 His Arg Pro Leu Leu Gly Arg Leu Ser Arg Gly Arg Pro Leu Ala Glu
 340 345 350
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 Asp Ala Ser
 30 370

 <210> 67
 <211> 90
 <212> PRT
 35 <213> Homo sapiens

Met Phe His Gln Ile Trp Ala Ala Leu Leu Tyr Phe Tyr Gly Ile Ile

15

<213> Homo sapiens

20

Met Val Asp Arg Gly Pro Leu Leu Thr Ser Ala Ile Ile Phe Tyr Leu

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	Ile	Phe	Glu	Val	Leu
	Glu	Glu	Pro	His	Trp
	Lys				
25	20	25	30		
	Glu	Ala	Lys	Lys	Asn
	Tyr	Tyr	Thr	Gln	Lys
	Leu	His	Leu	Leu	Lys
	Glu				
	35	40	45		
	Phe	Pro	Cys	Leu	Gly
	Gln	Glu	Gly	Leu	Asp
	Lys	Ile	Leu	Glu	Val
	Val				
	50	55	60		
30	Ser	Asp	Ala	Ala	Gly
	Gln	Gly	Val	Ala	Ile
	Thr	Gly	Asn	Gln	Thr
	Phe				
	65	70	75	80	
	Asn	Asn	Trp	Asn	Trp
	Pro	Asn	Ala	Met	Ile
	Phe	Ala	Ala	Thr	Val
	Ile				
	85	90	95		
	Thr	Thr	Ile	Gly	Tyr
	Gly	Asn	Val	Ala	Pro
	Lys	Thr	Pro	Ala	Gly
	Arg				
35	100	105	110		

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Leu Phe Cys Val Phe Tyr Gly Leu Phe Gly Val Pro Leu Cys Leu Thr
 115 120 125
 Trp Ile Ser Ala Leu Gly Lys Phe Phe Gly Gly Arg Ala Lys Arg Leu
 130 135 140
 5 Gly Gln Phe Leu Thr Lys Arg Gly Val Ser Leu Arg Lys Ala Gln Ile
 145 150 155 160
 Thr Cys Thr Val Ile Phe Ile Val Trp Gly Val Leu Val His Leu Val
 165 170 175
 Ile Pro Pro Phe Val Phe Met Val Thr Glu Gly Trp Asn Tyr Ile Glu
 10 180 185 190
 Gly Leu Tyr Tyr Ser Phe Ile Thr Ile Ser Thr Ile Gly Phe Gly Asp
 195 200 205
 Phe Val Ala Gly Val Asn Pro Ser Ala Asn Tyr His Ala Leu Tyr Arg
 210 215 220
 15 Tyr Phe Val Glu Leu Trp Ile Tyr Leu Gly Leu Ala Trp Leu Ser Leu
 225 230 235 240
 Phe Val Asn Trp Lys Val Ser Met Phe Val Glu Val His Lys Ala Ile
 245 250 255
 Lys Lys Arg Arg Arg Arg Arg Lys Glu Ser Phe Glu Ser Ser Pro His
 20 260 265 270
 Ser Arg Lys Ala Leu Gln Val Lys Gly Ser Thr Ala Ser Lys Asp Val
 275 280 285
 Asn Ile Phe Ser Phe Leu Ser Lys Lys Glu Glu Thr Tyr Asn Asp Leu
 290 295 300
 25 Ile Lys Gln Ile Gly Lys Lys Ala Met Lys Thr Ser Gly Gly Gly Glu
 305 310 315 320
 Thr Gly Pro Gly Pro Gly Leu Gly Pro Gln Gly Gly Gly Leu Pro Ala
 325 330 335
 Leu Pro Pro Ser Leu Val Pro Leu Val Val Tyr Ser Lys Asn Arg Val
 30 340 345 350
 Pro Thr Leu Glu Glu Val Ser Gln Thr Leu Arg Ser Lys Gly His Val
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 35 Ser Pro Ala Pro Glu Val Phe Met Asn Gln Leu Asp Arg Ile Ser Glu

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105

<211> 152

5 <212> PRT

<213> Homo sapiens

<400> 70

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35 40 45

15 Ser Leu Phe Leu Ile Ile Ser Met Cys Leu Leu Phe Leu Trp Lys Lys

50 55 60

Tyr Gln Pro Tyr Lys Val Ile Lys Gln Lys Leu Glu Gly Arg Pro Glu

65 70 75 80

Thr Glu Tyr Arg Lys Ala Gln Thr Phe Ser Gly His Glu Asp Ala Leu

20 85 90 95

Asp Asp Phe Gly Ile Tyr Glu Phe Val Ala Phe Pro Asp Val Ser Gly

100 105 110

Val Ser Arg Ile Pro Ser Arg Ser Val Pro Ala Ser Asp Cys Val Ser

115 120 125

25 Gly Gln Asp Leu His Ser Thr Val Tyr Glu Val Ile Gln His Ile Pro

130 135 140

Ala Gln Gln Gln Asp His Pro Glu

145 150

30 <210> 71

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<212> DNA

<213> Homo sapiens

35 <400> 71

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cagtgttatt tacttgtcta ctacaccggc tggcggaatg tcaaatcttt tttgactttt 780
ggcttaatct gtctatgcaa catgtatctc tatgaactgc gcaacctctg gcagcttttc 840
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<210> 72

<211> 549

20 <212> DNA

<213> Homo sapiens

<400> 72

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gaccggatcc tggtaggaga gcgtgctgg gacatgcct tgggtccct caaacagatt 240
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	Met Ser Met Ile Leu Ser Ala Ser Val Ile Arg Val Arg Asp	
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	Gln Glu Cys Arg Lys Tyr Phe Lys Met Leu Ser Arg Lys Leu Ala Gln	
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30	ctt cct gat aga tgt aca ctg aaa act gga cat tat aac att aat ttt	251
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 Met Arg Ala Leu Pro Gly Leu Leu Glu Ala Arg Ala

15 1 5 10
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 Arg Thr Pro Arg Leu Leu Leu Leu Gln Cys Leu Leu Ala Ala Ala Arg

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 Pro Ser Ser Ala Asp Gly Ser Ala Pro Asp Ser Pro Phe Thr Ser Pro

25 30 35 40
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95 100 105
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	Trp Thr Lys Tyr	Gln Leu Phe	Leu Ala Gly	Leu Met Leu	Val Thr Gly		
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	Gly Cys Gly Gly	Ser Lys Glu	His Ser Phe	Gln His Pro	Phe Leu Gln		
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 Phe Pro Cys Leu Gly Gln Glu Gly Leu Asp Lys Ile Leu Glu Val Val

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 Ser Asp Ala Ala Gly Gln Gly Val Ala Ile Thr Gly Asn Gln Thr Phe
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	Leu Phe Cys Val Phe Tyr Gly Leu Phe Gly Val Pro Leu Cys Leu Thr	
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	Met Asp Tyr Val Cys Cys	
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	gct tac aac aac ata acc ggc agg caa gat gaa act cat ttc aca gtt	161
	Ala Tyr Asn Asn Ile Thr Gly Arg Gln Asp Glu Thr His Phe Thr Val	
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<400> 91

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	Cys	Asp	Glu	Cys	Pro	Asn	Val	Lys	Leu	Val	Asn	Glu	Glu	Arg	Thr	Leu
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Lys Leu Glu Ser Gly His Leu Pro Ser Met Gln Gln Leu Val Gln Ile
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Ala Arg Arg Val His Glu Leu Glu Arg Val Lys Arg Arg Cys Leu Glu
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 Gly Ile Ile Ser Val Pro Leu Ser Ile Gly Tyr Cys Ala Ser Lys His
 195 200 205
 Ala Leu Arg Gly Phe Phe Asn Gly Leu Arg Thr Glu Leu Ala Thr Tyr
 210 215 220
 15 Pro Gly Ile Ile Val Ser Asn Ile Cys Pro Gly Pro Val Gln Ser Asn
 225 230 235 240
 Ile Val Glu Asn Ser Leu Ala Gly Glu Val Thr Lys Thr Ile Gly Asn
 245 250 255
 Asn Gly Asp Gln Ser His Lys Met Thr Thr Ser Arg Cys Val Arg Leu
 20 260 265 270
 Met Leu Ile Ser Met Ala Asn Asp Leu Lys Glu Val Trp Ile Ser Glu
 275 280 285
 Gln Pro Phe Leu Leu Val Thr Tyr Leu Trp Gln Tyr Met Pro Thr Trp
 290 295 300
 25 Ala Trp Trp Ile Thr Asn Lys Met Gly Lys Lys Arg Ile Glu Asn Phe
 305 310 315 320
 Lys Ser Gly Val Asp Ala Asp Ser Ser Tyr Phe Lys Ile Phe Lys Thr
 325 330 335
 Lys His Asp
 30
 <210> 95
 <211> 487
 <212> PRT
 <213> Homo sapiens
 35

260 265 270

[illegible]


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      275              280              285
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    290                295                300
Asp Tyr Ala Thr Ser Lys Asp Ala Arg Glu Pro Val Val Gly Ala Arg
5   305                310                315                320
Tyr Ile Gln Thr Leu Lys Asp His Arg Pro Arg Met Val Trp Asp Ser
          325                330                335
Gln Ala Ser Glu His Phe Phe Glu Tyr Lys Lys Ser Arg Ser Gly Arg
          340                345                350
10  His Val Val Phe Tyr Pro Thr Leu Lys Ser Leu Gln Val Arg Leu Glu
     355                360                365
Leu Ala Arg Glu Leu Gly Val Gly Val Ser Ile Trp Glu Leu Gly Gln
     370                375                380
Gly Leu Asp Tyr Phe Tyr Asp Leu Leu
15  385                390

<210> 97
<211> 196
<212> PRT
20  <213> Homo sapience

<400> 97
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   1                  5                  10                  15
25  Pro Gly Met His Arg Pro Glu Ala Met Leu Leu Leu Leu Thr Leu Ala
     20                25                30
Leu Leu Gly Gly Pro Thr Trp Ala Gly Lys Met Tyr Gly Pro Gly Gly
     35                40                45
Gly Lys Tyr Phe Ser Thr Thr Glu Asp Tyr Asp His Glu Ile Thr Gly
30  50                55                60
Leu Arg Val Ser Val Gly Leu Leu Leu Val Lys Ser Val Gln Val Lys
   65                70                75                80
Leu Gly Asp Ser Trp Asp Val Lys Leu Gly Ala Leu Gly Gly Asn Thr
           85                90                95
35  Gln Glu Val Thr Leu Gln Pro Gly Glu Tyr Ile Thr Lys Val Phe Val

```

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100 105 110
 Ala Phe Gln Ala Phe Leu Arg Gly Met Val Met Tyr Thr Ser Lys Asp
 115 120 125
 Arg Tyr Phe Tyr Phe Gly Lys Leu Asp Gly Gln Ile Ser Ser Ala Tyr
 5 130 135 140
 Pro Ser Gln Glu Gly Gln Val Leu Val Gly Ile Tyr Gly Gln Tyr Gln
 145 150 155 160
 Leu Leu Gly Ile Lys Ser Ile Gly Phe Glu Trp Asn Tyr Pro Leu Glu
 165 170 175
 10 Glu Pro Thr Thr Glu Pro Pro Val Asn Leu Thr Tyr Ser Ala Asn Ser
 180 185 190
 Pro Val Gly Arg
 195
 15 <210> 98
 <211> 107
 <212> PRT
 <213> Homo sapience
 20 <400> 98
 Met Glu Gln Lys Leu Val Glu Glu Ile Leu Gln Ala Ile Thr Met Ser
 1 5 10 15
 Thr Asp Thr Gly Val Ser Leu Pro Ser Tyr Glu Glu Asp Gln Gly Ser
 20 25 30
 25 Lys Leu Ile Arg Lys Ala Lys Glu Ala Pro Phe Val Pro Val Gly Ile
 35 40 45
 Ala Gly Phe Ala Ala Ile Val Ala Tyr Gly Leu Tyr Lys Leu Lys Ser
 50 55 60
 Arg Gly Asn Thr Lys Met Ser Ile His Leu Ile His Met Arg Val Ala
 30 65 70 75 80
 Ala Glu Gly Phe Val Val Gly Ala Met Thr Val Gly Met Gly Tyr Ser
 85 90 95
 Met Tyr Arg Glu Phe Trp Ala Lys Pro Lys Pro
 100 105
 35

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<210> 99

<211> 350

<212> PRT

<213> Homo sapience

5

<400> 99

Met Ser Glu Val Lys Ser Arg Lys Lys Ser Gly Pro Lys Gly Ala Pro
 1 5 10 15
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 10 20 25 30
 Arg Ser Ser Gly Gly Gly Gly Trp Ala Asp Pro Arg Thr Cys Leu Ser
 35 40 45
 Leu Leu Ser Leu Gly Thr Cys Leu Gly Leu Ala Trp Phe Val Phe Gln
 50 55 60
 15 Gln Ser Glu Lys Phe Ala Lys Val Glu Asn Gln Tyr Gln Leu Leu Lys
 65 70 75 80
 Leu Glu Thr Asn Glu Phe Gln Gln Leu Gln Ser Lys Ile Ser Leu Ile
 85 90 95
 Ser Glu Lys Trp Gln Lys Ser Glu Ala Ile Met Glu Gln Leu Lys Ser
 20 100 105 110
 Phe Gln Ile Ile Ala His Leu Lys Arg Leu Gln Glu Glu Ile Asn Glu
 115 120 125
 Val Lys Thr Trp Ser Asn Arg Ile Thr Glu Lys Gln Asp Ile Leu Asn
 130 135 140
 25 Asn Ser Leu Thr Thr Leu Ser Gln Asp Ile Thr Lys Val Asp Gln Ser
 145 150 155 160
 Thr Thr Ser Met Ala Lys Asp Val Gly Leu Lys Ile Thr Ser Val Lys
 165 170 175
 Thr Asp Ile Arg Arg Ile Ser Gly Leu Val Thr Asp Val Ile Ser Leu
 30 180 185 190
 Thr Asp Ser Val Gln Glu Leu Glu Asn Lys Ile Glu Lys Val Glu Lys
 195 200 205
 Asn Thr Val Lys Asn Ile Gly Asp Leu Leu Ser Ser Ser Ile Asp Arg
 210 215 220
 35 Thr Ala Thr Leu Arg Lys Thr Ala Ser Glu Asn Ser Gln Arg Ile Asn

	225		230		235		240
	Ser Val Lys Lys Thr Leu Thr Glu Leu Lys Ser Asp Phe Asp Lys His						
	245		250		255		
	Thr Asp Arg Phe Leu Ser Leu Glu Gly Asp Arg Ala Lys Val Leu Lys						
5	260		265		270		
	Thr Val Thr Phe Ala Asn Asp Leu Lys Pro Lys Val Tyr Asn Leu Lys						
	275		280		285		
	Lys Asp Phe Ser Arg Leu Glu Pro Leu Val Asn Asp Leu Thr Leu Arg						
	290		295		300		
10	Ile Gly Arg Leu Val Thr Asp Leu Leu Gln Arg Glu Lys Glu Ile Ala						
	305		310		315		320
	Phe Leu Ser Glu Lys Ile Ser Asn Leu Thr Ile Val Gln Ala Glu Ile						
	325		330		335		
	Lys Asp Ile Lys Asp Glu Ile Ala His Ile Ser Asp Met Asn						
15	340		345		350		
	<210> 100						
	<211> 107						
	<212> PRT						
20	<213> Homo sapience						
	<400> 100						
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25	Thr Ser Gln Pro Gly Arg Pro Ser Phe Tyr Cys Asn Ser Arg His Ser						
	20		25		30		
	Ile Val Gly Ser Ser His Gln Leu Gly Phe Trp Phe Ser His Leu Glu						
	35		40		45		
	Ser Ser Gly Leu Lys Val Phe Gln Val Ser Leu Pro Cys Glu Cys Val						
30	50		55		60		
	Asn Leu Pro Thr Arg Ile Ala Ser Val Val Leu Ser Leu Met Ser Leu						
	65		70		75		80
	Leu Val Val Gly Gln Ala Pro Ala Trp Glu Gly Ser Leu Leu Arg Gly						
	85		90		95		
35	Arg Pro Ala Gly Gly Ala His Leu Cys Ala Ala						

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100

105

<210> 101

<211> 1074

5

<212> DNA

<213> Homo Sapience

<400> 101

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	attaaaaagg cctataggaa actagccctg cagcttcac cgcaccggaa cctgatgat	180
	ccacaagccc aggagaaatt ccaggatctg ggtgctgctt atgaggttct gtcagatagt	240
	gagaaacgga aacagtacga tacttatggt gaagaaggat taaaagatgg tcatcagagc	300
	tcccatggag acattttttc acacttcttt ggggattttg gtttcatgtt tggaggaacc	360
15	cctcgtcagc aagacagaaa tattccaaga ggaagtgata ttattgtaga tctagaagtc	420
	acttttgaag aagtatatgc aggaaatfff gtggaagtag ttagaaacaa acctgtggca	480
	aggcaggctc ctggcaaacg gaagtgcaat tgctggcaag agatgcggac caccagctg	540
	ggccctgggc gcttccaaat gaccagggag gtggtctcg acgaatgccc taatgtcaaa	600
	ctagtgaatg aagaacgaac gctggaagta gaaatagagc ctgggggtgag agacggcatg	660
20	gagtaccctt ttattggaga aggtgagcct cacgtggatg gggagcctgg agatttacgg	720
	ttccgaatca aagttgtcaa gcaccaata tttgaaagga gaggagatga tttgtacaca	780
	aatgtgacaa tctcattagt tgagtcactg gttggctttg agatggatat tactcacttg	840
	gatggtcaca aggtacatat ttcccgggat aagatcacca ggccaggagc gaagctatgg	900
	aagaaagggg aagggctccc caactttgac aacaacaata tcaagggctc tttgataatc	960
25	acttttgatg tggattttcc aaaagaacag ttaacagagg aagcgagaga aggtatcaaa	1020
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<210> 102

<211> 678

30

<212> DNA

<213> Homo Sapience

<400> 102

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5 ttgattttat tgagtgcctt ggetgatccg gatcagtata acttttcaag ttctgaactg 180
 ggaggtgact ttgagttcat ggatgatgcc aacatgtgca ttgccattgc gatttctctt 240
 ctcatgatcc tgatatgtgc tatggctact tacggagcgt acaagcaacg cgcagcctgg 300
 atcatcccat tcttctgtta ccagatcttt gactttgccc tgaacatgtt ggttgcaatc 360
 actgtgctta tttatccaaa ctccattcag gaatacatat ggcaactgcc tcctaatttt 420
 ccctacagag atgatgtcat gtcagtgaat cctacctgtt tggctcctat tattcttctg 480
 tttattagca ttatcttgac ttttaagggg taacttgatta gctgtgtttg gaactgctac 540
 cgatacatca atggtaggaa ctctctgat gtcctggttt atgttaccag caatgacaact 600
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 10 ccacettacg tgtctgcc 678

<210> 103

<211> 585

<212> DNA

15 <213> Homo Sapience

<400> 103

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 20 ctcaagttcc agatttgtgt ttcctgaggt tataggcggg tgtttgagga gtacatgcgg 180
 gttattagcc agcgggtacc agacatccgc attgaaggag agaattacct cctcaacca 240
 atatatagac acatagcatc tttcctgtca gtcttcaaac tagtattaat aggettaata 300
 attgttggca aggatccttt tgccttcttt ggcattgcaag ctctagcat ctggcagtgg 360
 ggccaagaaa ataaggttta tgcattgatg atggttttct tcttgagcaa catgattgag 420
 25 aaccagtgtg tgtcaacagg tgcatttgag ataaacttta atgatgtacc tgtgtggtct 480
 aagctggaat ctggtcacct tccatccatg caacaacttg ttcaaattct tgacaatgaa 540
 atgaagctca atgtgcatat ggattcaatc ccacaccatc gatca 585

<210> 104

30 <211> 1017

<212> DNA

<213> Homo Sapience

<400> 104

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	agcagcttct tctacagaca caaagatagt cggatatctga cgccgctggt ctgcctcagc	780
	tttgcggtc tgacccagc gtgggtcctc attgccaagc agagcccacc catcgtgaag	840
	atcctgaagt ttggtggtt cccaatcacc ctggccatgg tcatcagcag ttctggagga	900
	ctcatcttga gcaaaaccgt ttctaaacag cagtacaaag gcatggcgat atttaccccc	960
5	gtcatatgtg gtgttggtg caatctggtg gccattcaga ccagccgaat ctcaacctac	1020
	ctgcacatgt ggagtgcacc tggcgtcctg cccctccaga tgaagaaatt ctggcccaac	1080
	ccgtgttcta ctttctgcac gtcagaaatc aattccatgt cagctcgagt cctgctcttg	1140
	ctggtggtcc caggccatct gattttcttc tacatcatct acctggtgga gggtcagtca	1200
	gtcataaaca gccagacctt tgtggtgctc tacctgctgg caggcctgat ccaggtgaca	1260
10	atcctgctgt acctggcaga agtgatggtt cggtgactt ggcaccaggc cctggatcct	1320
	gacaaccact geatcccta ccttacaggg ctgggggacc tgctcggtac tggcctcctg	1380
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	gaactggcat ctggacctcc c	1461
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	<211> 1179	
	<212> DNA	
	<213> Homo Sapience	
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	ctgtcaaagt cagatgccaa aaaagccgcc tcaaagacgc tgctggagaa gagtcagttt	120
	tcagataagc cgggtgcaaga ccgggggttg gtggtgacgg acctcaaagc tgagagtgtg	180
	gtttctgagc atcgcagcta ctgctcggca aaggcccgga acagacactt tgctggggat	240
25	gtactgggct atgtcactcc atggaacagc catggctacg atgtcaccaa ggtctttggg	300
	agcaagttca cacagatctc acccgtctgg ctgcagctga agagacgtgg ccgtgagatg	360
	tttgaggtca cgggcctcca cgacgtggac caagggtgga tgcgagctgt caggaagcat	420
	gccaaagggc tgcacatagt gcctcggctc ctgtttgagg actggactta cgatgatttc	480
	cggaacgtct tagacagtga ggatgagata gaggagctga gcaagaccgt ggtccagggtg	540
30	gcaaagaacc agcatttoga ttgcttcgtg gtggaggtct ggaaccagct gctaagccag	600
	aagcgggtgg gcctcatcca catgctcacc cacttgcccg aggetctgca ccaggcccg	660
	ctgtggccc tcttggtcat cccgcctgcc atcacccccc ggaccgacca gctgggcatg	720
	ttcacgcaca aggagtttga gcagctggcc cccgtgctgg atggtttcag cctcatgacc	780
	tacgactact ctacagcgca tcagcctggc cctaattgac ccctgtcctg ggttcagacc	840
35	tgcgtccagg tcttggaacc gaagtccaag tggcgaagca aaatcctcct ggggctcaac	900

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ttctatggta tggactacgc gacctccaag gatgcccggt agcctgttgt cggggccagg 960
 tacatccaga cactgaagga ccacaggccc cggatggtgt gggacagcca ggcctcagag 1020
 cactttcttcg agtacaagaa gagccgcagt gggaggcacg tcgtctteta cccaacctg 1080
 aagtccctgc aggtgcgggt ggagctggcc cgggagctgg gcgttggggt ctctatctgg 1140
 5 gagctggggc agggcctgga ctacttctac gacctgctc 1179

<210> 107

<211> 588

<212> DNA

10 <213> Homo Sapience

<400> 107

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 cggccagagg ccatgctgct gctgctcagc cttgccctcc tggggggccc cacctgggca 120
 15 gggaagatgt atggccctgg aggaggcaag tatttcagca cactgaaga ctacgaccat 180
 gaaatcacag ggctgcgggt gtctgtaggt cttctcctgg tgaaaagtgt ccaggtgaaa 240
 cttggagact cctgggacgt gaaactggga gccttaggtg ggaataccca ggaagtcacc 300
 ctgcagccag gcgaatacat caaaaagtc tttgtcgctc tocaagcttt cctccgggggt 360
 atggtcatgt acaccagcaa ggaccgctat ttctattttg ggaagcttga tggccagatc 420
 20 tcctctgcct accccagcca agaggggcag gtgctggtgg gcattctatgg ccagtatcaa 480
 ctcttgga tcaagagcat tggtttgaa tggaattatc cactagagga gccgaccact 540
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<210> 108

25 <211> 321

<212> DNA

<213> Homo Sapience

<400> 108

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 gcaccattcg taccggttg aatagcgggt tttgcagcaa ttgttcata tggattatat 180
 aaactgaaga gcaggggaaa tactaaaatg tccattcacc tgatccacat gcgtgtggca 240
 gcccaaggct ttgttgtagg agcaatgact gttggtatgg gctattccat gtatcgggaa 300
 35 ttctgggcaa aacctaagcc t 321

35 atgtcctcag caggcacagc aaccctcttg gaaatggatc acaaactcac ttctcagcca 60
ggcaggccaa gcttctattg taacagtagg cacagtatag tcggatcacc acatcagctg 120
ggtttttggg ttagtcattc agagtcgtct ggactaaagg tcttctcagg ctctcttgccc 180

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tgtgagtgcg tgaacctccc caccgaatt gcctcagttg tcctgagcct catgtctctc 240
 ctgggtggtgg gccaggcccc tgcattggaa gggagcctgc tgcggggcag gccagctggg 300
 ggtgctcacc tatgcgcagc a 321

5 <210> 111
 <211> 1619
 <212> DNA
 <213> Homo Sapience
 <220>

10 <221> CDS
 <222> (158)...(1234)

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 15 tgaggcgccc tcacagggcc ggggtgggctg gcgagccgac gcggcgggcg aggaggctgt 120
 gaggagtgtg tggaacagga ccggggacag aggaacc atg gct ccg cag aac ctg 175
 Met Ala Pro Gln Asn Leu
 1 5
 agc acc ttt tgc ctg ttg ctg cta tac ctc atc ggg gcg gtg att gcc 223
 20 Ser Thr Phe Cys Leu Leu Leu Tyr Leu Ile Gly Ala Val Ile Ala
 10 15 20
 gga cga gat ttc tat aag atc ttg ggg gtg cct cga agt gcc tct ata 271
 Gly Arg Asp Phe Tyr Lys Ile Leu Gly Val Pro Arg Ser Ala Ser Ile
 25 30 35
 25 aag gat att aaa aag gcc tat agg aaa cta gcc ctg cag ctt cat ccc 319
 Lys Asp Ile Lys Lys Ala Tyr Arg Lys Leu Ala Leu Gln Leu His Pro
 40 45 50
 gac cgg aac cct gat gat cca caa gcc cag gag aaa ttc cag gat ctg 367
 Asp Arg Asn Pro Asp Asp Pro Gln Ala Gln Glu Lys Phe Gln Asp Leu
 30 55 60 65 70
 ggt gct gct tat gag gtt ctg tca gat agt gag aaa cgg aaa cag tac 415
 Gly Ala Ala Tyr Glu Val Leu Ser Asp Ser Glu Lys Arg Lys Gln Tyr
 75 80 85
 gat act tat ggt gaa gaa gga tta aaa gat ggt cat cag agc tcc cat 463
 35 Asp Thr Tyr Gly Glu Glu Gly Leu Lys Asp Gly His Gln Ser Ser His

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	90	95	100	
	gga gac att ttt tca cac ttc ttt ggg gat ttt ggt ttc atg ttt gga			511
	Gly Asp Ile Phe Ser His Phe Phe Gly Asp Phe Gly Phe Met Phe Gly			
	105	110	115	
5	gga acc cct cgt cag caa gac aga aat att cca aga gga agt gat att			559
	Gly Thr Pro Arg Gln Gln Asp Arg Asn Ile Pro Arg Gly Ser Asp Ile			
	120	125	130	
	att gta gat cta gaa gtc act ttg gaa gaa gta tat gca gga aat ttt			607
	Ile Val Asp Leu Glu Val Thr Leu Glu Glu Val Tyr Ala Gly Asn Phe			
10	135	140	145	150
	gtg gaa gta gtt aga aac aaa cct gtg gca agg cag gct cct ggc aaa			655
	Val Glu Val Val Arg Asn Lys Pro Val Ala Arg Gln Ala Pro Gly Lys			
	155	160	165	
	cgg aag tgc aat tgt cgg caa gag atg cgg acc acc cag ctg ggc cct			703
15	Arg Lys Cys Asn Cys Arg Gln Glu Met Arg Thr Thr Gln Leu Gly Pro			
	170	175	180	
	ggg cgc ttc caa atg acc cag gag gtg gtc tgc gac gaa tgc cct aat			751
	Gly Arg Phe Gln Met Thr Gln Glu Val Val Cys Asp Glu Cys Pro Asn			
	185	190	195	
20	gtc aaa cta gtg aat gaa gaa cga acg ctg gaa gta gaa ata gag cct			799
	Val Lys Leu Val Asn Glu Glu Arg Thr Leu Glu Val Glu Ile Glu Pro			
	200	205	210	
	ggg gtg aga gac ggc atg gag tac ccc ttt att gga gaa ggt gag cct			847
	Gly Val Arg Asp Gly Met Glu Tyr Pro Phe Ile Gly Glu Gly Glu Pro			
25	215	220	225	230
	cac gtg gat ggg gag cct gga gat tta cgg ttc cga atc aaa gtt gtc			895
	His Val Asp Gly Glu Pro Gly Asp Leu Arg Phe Arg Ile Lys Val Val			
	235	240	245	
	aag cac cca ata ttt gaa agg aga gga gat gat ttg tac aca aat gtg			943
30	Lys His Pro Ile Phe Glu Arg Arg Gly Asp Asp Leu Tyr Thr Asn Val			
	250	255	260	
	aca atc tca tta gtt gag tca ctg gtt ggc ttt gag atg gat att act			991
	Thr Ile Ser Leu Val Glu Ser Leu Val Gly Phe Glu Met Asp Ile Thr			
	265	270	275	
35	cac ttg gat ggt cac aag gta cat att tcc cgg gat aag atc acc agg			1039

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His Leu Asp Gly His Lys Val His Ile Ser Arg Asp Lys Ile Thr Arg
 280 285 290
 cca gga gcg aag cta tgg aag aaa ggg gaa ggg ctc ccc aac ttt gac 1087
 Pro Gly Ala Lys Leu Trp Lys Lys Gly Glu Gly Leu Pro Asn Phe Asp
 5 295 300 305 310
 aac aac aat atc aag ggc tct ttg ata atc act ttt gat gtg gat ttt 1135
 Asn Asn Asn Ile Lys Gly Ser Leu Ile Ile Thr Phe Asp Val Asp Phe
 315 320 325
 cca aaa gaa cag tta aca gag gaa gcg aga gaa ggt atc aaa cag cta 1183
 10 Pro Lys Glu Gln Leu Thr Glu Glu Ala Arg Glu Gly Ile Lys Gln Leu
 330 335 340
 ctg aaa caa ggg tca gtg cag aag gta tac aat gga ctg caa gga tat 1231
 Leu Lys Gln Gly Ser Val Gln Lys Val Tyr Asn Gly Leu Gln Gly Tyr
 345 350 355
 15 tgagagtga ataaaattgg actttgttta aaataagtga ataagcgata tttattatct 1290
 gcaagggtttt tttgtgtgtg tttttgtttt tatttttcaat atgcaagtta ggcttaattt 1350
 ttttatctaa tgatcatcat gaaatgaata agagggctta agaatttgct catttgcat 1410
 cggaagaa tgaccagcaa aaggtttact aatacctctc cctttgggga tttaatgtct 1470
 ggtgctgccg cctgagtttc aagaattaaa gctgcaagag gactccagga gcaaaagaaa 1530
 20 cacaatatag aggggttgag ttgtagcaa ttccattcaa aatgccaact ggagaagtct 1590
 gtttttaaat acattttgtt gttattttt 1619

 <210> 112
 <211> 2054
 25 <212> DNA
 <213> Homo Sapience
 <220>
 <221> CDS
 <222> (254)...(934)
 30
 <400> 112
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 gcggggcgac gggcgagcgg gccgggagcc ggagcgggcg aggagccggc agcagcggcg 180
 35 cggcgggctc caggcgaggc ggtcgacgct cctgaaaact tgcgcgcgcg ctcgcgccac 240

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	tgcgcccgga gcg atg aag atg gtc gcg ccc tgg acg cgg ttc tac tcc	289
	Met Lys Met Val Ala Pro Trp Thr Arg Phe Tyr Ser	
	1 5 10	
	aac agc tgc tgc ttg tgc tgc cat gtc cgc acc ggc acc atc ctg ctc	337
5	Asn Ser Cys Cys Leu Cys Cys His Val Arg Thr Gly Thr Ile Leu Leu	
	15 20 25	
	ggc gtc tgg tat ctg atc atc aat gct gtg gta ctg ttg att tta ttg	385
	Gly Val Trp Tyr Leu Ile Ile Asn Ala Val Val Leu Leu Ile Leu Leu	
	30 35 40	
10	agt gcc ctg gct gat ccg gat cag tat aac ttt tca agt tct gaa ctg	433
	Ser Ala Leu Ala Asp Pro Asp Gln Tyr Asn Phe Ser Ser Ser Glu Leu	
	45 50 55 60	
	gga ggt gac ttt gag ttc atg gat gat gcc aac atg tgc att gcc att	481
	Gly Gly Asp Phe Glu Phe Met Asp Asp Ala Asn Met Cys Ile Ala Ile	
15	65 70 75	
	gcg att tct ctt ctc atg atc ctg ata tgt gct atg gct act tac gga	529
	Ala Ile Ser Leu Leu Met Ile Leu Ile Cys Ala Met Ala Thr Tyr Gly	
	80 85 90	
	gcg tac aag caa cgc gca gcc tgg atc atc cca ttc ttc tgt tac cag	577
20	Ala Tyr Lys Gln Arg Ala Ala Trp Ile Ile Pro Phe Phe Cys Tyr Gln	
	95 100 105	
	atc ttt gac ttt gcc ctg aac atg ttg gtt gca atc act gtg ctt att	625
	Ile Phe Asp Phe Ala Leu Asn Met Leu Val Ala Ile Thr Val Leu Ile	
	110 115 120	
25	tat cca aac tcc att cag gaa tac ata cgg caa ctg cct cct aat ttt	673
	Tyr Pro Asn Ser Ile Gln Glu Tyr Ile Arg Gln Leu Pro Pro Asn Phe	
	125 130 135 140	
	ccc tac aga gat gat gtc atg tca gtg aat cct acc tgt ttg gtc ctt	721
	Pro Tyr Arg Asp Asp Val Met Ser Val Asn Pro Thr Cys Leu Val Leu	
30	145 150 155	
	att att ctt ctg ttt att agc att atc ttg act ttt aag ggt tac ttg	769
	Ile Ile Leu Leu Phe Ile Ser Ile Ile Leu Thr Phe Lys Gly Tyr Leu	
	160 165 170	
	att agc tgt gtt tgg aac tgc tac cga tac atc aat ggt agg aac tcc	817
35	Ile Ser Cys Val Trp Asn Cys Tyr Arg Tyr Ile Asn Gly Arg Asn Ser	

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<221> CDS

<222> (43)...(630)

<400> 113

5	gcagctctgtc tgagggcggc cgaagtggct ggctcattta ag atg agg ctt ctg	54
	Met Arg Leu Leu	
	1	
	ctg ctt ctc cta gtg gcg gcg tct gcg atg gtc cgg agc gag gcc tcg	102
	Leu Leu Leu Leu Val Ala Ala Ser Ala Met Val Arg Ser Glu Ala Ser	
10	5 10 15 20	
	gcc aat ctg ggc ggc gtg ccc agc aag aga tta aag atg cag tac gcc	150
	Ala Asn Leu Gly Gly Val Pro Ser Lys Arg Leu Lys Met Gln Tyr Ala	
	25 30 35	
	acg ggg ccg ctg ctc aag ttc cag att tgt gtt tcc tga ggt tat agg	198
15	Thr Gly Pro Leu Leu Lys Phe Gln Ile Cys Val Ser Xaa Gly Tyr Arg	
	40 45 50	
	cgg gtg ttt gag gag tac atg cgg gtt att agc cag cgg tac cca gac	246
	Arg Val Phe Glu Glu Tyr Met Arg Val Ile Ser Gln Arg Tyr Pro Asp	
	55 60 65	
20	atc cgc att gaa gga gag aat tac ctc cct caa cca ata tat aga cac	294
	Ile Arg Ile Glu Gly Glu Asn Tyr Leu Pro Gln Pro Ile Tyr Arg His	
	70 75 80	
	ata gca tct ttc ctg tca gtc ttc aaa cta gta tta ata ggc tta ata	342
	Ile Ala Ser Phe Leu Ser Val Phe Lys Leu Val Leu Ile Gly Leu Ile	
25	85 90 95 100	
	att gtt ggc aag gat cct ttt gct ttc ttt ggc atg caa gct cct agc	390
	Ile Val Gly Lys Asp Pro Phe Ala Phe Phe Gly Met Gln Ala Pro Ser	
	105 110 115	
	atc tgg cag tgg ggc caa gaa aat aag gtt tat gca tgt atg atg gtt	438
30	Ile Trp Gln Trp Gly Gln Glu Asn Lys Val Tyr Ala Cys Met Met Val	
	120 125 130	
	ttc ttc ttg agc aac atg att gag aac cag tgt atg tca aca ggt gca	486
	Phe Phe Leu Ser Asn Met Ile Glu Asn Gln Cys Met Ser Thr Gly Ala	
	135 140 145	
35	ttt gag ata act tta aat gat gta cct gtg tgg tct aag ctg gaa tct	534

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Phe Glu Ile Thr Leu Asn Asp Val Pro Val Trp Ser Lys Leu Glu Ser
 150 155 160
 ggt cac ctt cca tcc atg caa caa ctt gtt caa att ctt gac aat gaa 582
 Gly His Leu Pro Ser Met Gln Gln Leu Val Gln Ile Leu Asp Asn Glu
 5 165 170 175 180
 atg aag ctc aat gtg cat atg gat tca atc cca cac cat cga tca 627
 Met Lys Leu Asn Val His Met Asp Ser Ile Pro His His Arg Ser
 185 190 195
 tag caccacctat cagcactgaa aactcttttg cattaaggga tcattgcaag 680
 10 agcagcgtga ctgacattat gaaggcctgt actgaagaca gcaagctgtt agtacagacc 740
 agatgetttc ttggcaggct cgttgtacct cttggaaaac ctcaatgcaa gatagtgttt 800
 cagtgetggc atattttgga attctgcaca ttcattggagt gcaataatac tgtatagctt 860
 tccccacctc ccacaaaatc acccagttaa tgtgtgtgtg tgtttttttt ttttaaggtaa 920
 acattactac ttgtaaacttt ttttcttagt catatttgaa aaagtagaaa attgagttac 980
 15 aatttgattt tttttccaaa gatgtctgtt aaatctgttg tgcttttata tgaatatttg 1040
 ttttttatag tttaaaattg atcctttggg aatccagttg aagttcccaa atactttata 1100
 agagtttato agacatctct aatttggtcca tgtccagttt atacagttta caaaatatag 1160
 cagatgcaag attatggggg aaatcctata ttcagagtac tctataaatt tttgtgtatg 1220
 tgtgtatgtg cgtgtgatta ccagagaact actaaaaaaa ccaactgctt tttaaatcct 1280
 20 attgtgtagt taaagtgtca tgccttgacc aatctaataa attgattaat taactgggcc 1340
 tttatactta actaaataaa aaactaagca gatatgagtt 1380

<210> 114
 <211> 1292
 25 <212> DNA
 <213> Homo Sapience
 <220>
 <221> CDS
 <222> (113)...(1132)

30
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 gactctggtg cgggccgtct tcttcccccc gagctggggg tgcgcggccg ca atg aac 118

Met Asn

35

1

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	180	185	190	
	ata tct gta cct ctt tcc att gga tac tgt gct agc aag cat gct ctc			742
	Ile Ser Val Pro Leu Ser Ile Gly Tyr Cys Ala Ser Lys His Ala Leu			
	195	200	205	210
5	cgg ggt ttt ttt aat ggc ctt cga aca gaa ctt gcc aca tac cca ggt			790
	Arg Gly Phe Phe Asn Gly Leu Arg Thr Glu Leu Ala Thr Tyr Pro Gly			
	215	220	225	
	ata ata gtt tct aac att tgc cca gga cct gtg caa tca aat att gtg			838
	Ile Ile Val Ser Asn Ile Cys Pro Gly Pro Val Gln Ser Asn Ile Val			
10	230	235	240	
	gag aat tcc cta gct gga gaa gtc aca aag act ata ggc aat aat gga			886
	Glu Asn Ser Leu Ala Gly Glu Val Thr Lys Thr Ile Gly Asn Asn Gly			
	245	250	255	
	gac cag tcc cac aag atg aca acc agt cgt tgt gtg cgg ctg atg tta			934
15	Asp Gln Ser His Lys Met Thr Thr Ser Arg Cys Val Arg Leu Met Leu			
	260	265	270	
	atc agc atg gcc aat gat ttg aaa gaa gtt tgg atc tca gaa caa cct			982
	Ile Ser Met Ala Asn Asp Leu Lys Glu Val Trp Ile Ser Glu Gln Pro			
	275	280	285	290
20	ttc ttg tta gta aca tat ttg tgg caa tac atg cca acc tgg gcc tgg			1030
	Phe Leu Leu Val Thr Tyr Leu Trp Gln Tyr Met Pro Thr Trp Ala Trp			
	295	300	305	
	tgg ata acc aac aag atg ggg aag aaa agg att gag aac ttt aag agt			1078
	Trp Ile Thr Asn Lys Met Gly Lys Lys Arg Ile Glu Asn Phe Lys Ser			
25	310	315	320	
	ggt gtg gat gca gac tct tct tat ttt aaa atc ttt aag aca aaa cat			1126
	Gly Val Asp Ala Asp Ser Ser Tyr Phe Lys Ile Phe Lys Thr Lys His			
	325	330	335	
	gac tgaaaagagc atctgtactt ttcaagccac tggaggggaaa aatggaaaac a			1180
30	Asp			
	tgaaaacagc aatcttctta tgcttctgaa taatcaaaga ctaatttggtg gttttacttt			1240
	ttaatagata tgactttgct tccaacatgg aatgaaataa aaaataagta at			1292
35	<210> 115			

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	130	135	140	
	agc aac ctg gcc ctc atc cag gtg cag gcc act gtc gtg ggg ctc ttg			535
	Ser Asn Leu Ala Leu Ile Gln Val Gln Ala Thr Val Val Gly Leu Leu			
	145	150	155	160
5	gct gct gtg gct gcg ctg ctg ttg ggc gtg gtg tct cga gag gaa gtg			583
	Ala Ala Val Ala Ala Leu Leu Leu Gly Val Val Ser Arg Glu Glu Val			
	165	170	175	
	gat gtc gcc aag gtg gag ttg ctg tgt gcc agc agt gtc ctc act gcc			631
	Asp Val Ala Lys Val Glu Leu Leu Cys Ala Ser Ser Val Leu Thr Ala			
10	180	185	190	
	ttc ctt gca gcc ttt gcc ctg ggg gtg ctg atg gtc tgt ata gtg att			679
	Phe Leu Ala Ala Phe Ala Leu Gly Val Leu Met Val Cys Ile Val Ile			
	195	200	205	
	ggc gct cga aag ctc ggg gtc aac cca gac aac att gcc acg ccc att			727
15	Gly Ala Arg Lys Leu Gly Val Asn Pro Asp Asn Ile Ala Thr Pro Ile			
	210	215	220	
	gca gcc agc ctg gga gac ctc atc aca ctg tcc att ctg gct ttg gtt			775
	Ala Ala Ser Leu Gly Asp Leu Ile Thr Leu Ser Ile Leu Ala Leu Val			
	225	230	235	240
20	agc agc ttc ttc tac aga cac aaa gat agt cgg tat ctg acg ccg ctg			823
	Ser Ser Phe Phe Tyr Arg His Lys Asp Ser Arg Tyr Leu Thr Pro Leu			
	245	250	255	
	gtc tgc ctc agc ttt gcg gct ctg acc cca gtg tgg gtc ctc att gcc			871
	Val Cys Leu Ser Phe Ala Ala Leu Thr Pro Val Trp Val Leu Ile Ala			
25	260	265	270	
	aag cag agc cca ccc atc gtg aag atc ctg aag ttt ggc tgg ttc cca			919
	Lys Gln Ser Pro Pro Ile Val Lys Ile Leu Lys Phe Gly Trp Phe Pro			
	275	280	285	
	atc atc ctg gcc atg gtc atc agc agt ttc gga gga ctc atc ttg agc			967
30	Ile Ile Leu Ala Met Val Ile Ser Ser Phe Gly Gly Leu Ile Leu Ser			
	290	295	300	
	aaa acc gtt tct aaa cag cag tac aaa ggc atg gcg ata ttt acc ccc			1015
	Lys Thr Val Ser Lys Gln Gln Tyr Lys Gly Met Ala Ile Phe Thr Pro			
	305	310	315	320
35	gtc ata tgt ggt gtt ggt ggc aat ctg gtg gcc att cag acc agc cga			1063

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130/177

gagtgtgtga atatgatgtg tgcacatgct taatgagcgt gcaagtgtgc acacgtttgt 1790
 ggagaggagg gtgttctggc ctgagaagct aaagaagagg catgtccagt atgcttttgc 1850
 ggggtgtgtt gctcttttcc atgcccattg aaccagatt ggggtggagc aggaaggagc 1910
 tcttttctgt tcccaagcct cagaactctt gagctgtggc ttacttgcctg tcttcaccag 1970
 5 gttcaagctc cgtggggccac actgctgctg tgccaagaag gtgtacagcc tccccaggat 2030
 ggggcctcat acaacccttc atctgcactc aacatttaat cgtgtccttg ctgtcttttt 2090
 attttccttt ttgttagcaa aaacctatat ttagatttca ataatacagag aagtgtaaaa 2150
 taaaacagat tatattgt 2168

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 <211> 1357
 <212> DNA
 <213> Homo Sapience
 <220>

15 <221> CDS
 <222> (81)...(1262)

<400> 116

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 cctactgtga cacacctacc atg cgg aca etc ttc aac etc etc tgg ctt 110
 Met Arg Thr Leu Phe Asn Leu Leu Trp Leu
 1 5 10
 gcc ctg gcc tgc agc cct gtt cac act acc ctg tca aag tca gat gcc 158
 Ala Leu Ala Cys Ser Pro Val His Thr Thr Leu Ser Lys Ser Asp Ala
 15 20 25
 25 aaa aaa gcc gcc tca aag acg ctg ctg gag aag agt cag ttt tca gat 203
 Lys Lys Ala Ala Ser Lys Thr Leu Leu Glu Lys Ser Gln Phe Ser Asp
 30 35 40
 aag ccg gtg caa gac cgg ggt ttg gtg gtg acg gac etc aaa gct gag 254
 30 Lys Pro Val Gln Asp Arg Gly Leu Val Val Thr Asp Leu Lys Ala Glu
 45 50 55
 agt gtg gtt ctt gag cat cgc agc tac tgc tgc gca aag gcc cgg gac 302
 Ser Val Val Leu Glu His Arg Ser Tyr Cys Ser Ala Lys Ala Arg Asp
 60 65 70
 35 aga cac ttt gct ggg gat gta ctg ggc tat gtc act cca tgg aac agc 350

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cat cag cct ggc cct aat gca ccc ctg tcc tgg gtt cga gcc tgc gtc 926
 His Gln Pro Gly Pro Asn Ala Pro Leu Ser Trp Val Arg Ala Cys Val
 270 275 280

cag gtc ctg gac ccg aag tcc aag tgg cga agc aaa atc ctc ctg ggg 974
 5 Gln Val Leu Asp Pro Lys Ser Lys Trp Arg Ser Lys Ile Leu Leu Gly
 285 290 295

ctc aac ttc tat ggt atg gac tac gcg acc tcc aag gat gcc cgt gag 1022
 Leu Asn Phe Tyr Gly Met Asp Tyr Ala Thr Ser Lys Asp Ala Arg Glu
 300 305 310

cct gtt gtc ggg gcc agg tac atc cag aca ctg aag gac cac agg ccc 1070
 10 Pro Val Val Gly Ala Arg Tyr Ile Gln Thr Leu Lys Asp His Arg Pro
 315 320 325 330

cgg atg gtg tgg gac agc cag gcc tca gag cac ttc ttc gag tac aag 1118
 Arg Met Val Trp Asp Ser Gln Ala Ser Glu His Phe Phe Glu Tyr Lys
 15 335 340 345

aag agc cgc agt ggg agg cac gtc gtc ttc tac cca acc ctg aag tcc 1166
 Lys Ser Arg Ser Gly Arg His Val Val Phe Tyr Pro Thr Leu Lys Ser
 350 355 360

ctg cag gtg cgg ctg gag ctg gcc cgg gag ctg ggc gtt ggg gtc tct 1214
 20 Leu Gln Val Arg Leu Glu Leu Ala Arg Glu Leu Gly Val Gly Val Ser
 365 370 375

atc tgg gag ctg ggc cag ggc ctg gac tac ttc tac gac ctg ctc t 1260
 Ile Trp Glu Leu Gly Gln Gly Leu Asp Tyr Phe Tyr Asp Leu Leu
 380 385 390

aggtgggcat tgcggcctcc gcggtggagc tgttcttttc taagccatgg agtgagtgag 1320
 25 caggtgtgaa atacaggcct ccactccggt tgcgtgtg 1357

<210> 117

<211> 711

30 <212> DNA

<213> Homo Sapience

<220>

<221> CDS

<222> (8)...(598)

35

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133/177

<400> 117

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	Met Trp Arg Val Pro Gly Thr Thr Arg Arg Pro Val Thr Gly	
	1 5 10	
5	gag agc cct ggg atg cac cgg cca gag gcc atg ctg ctg ctg ctc acg	97
	Glu Ser Pro Gly Met His Arg Pro Glu Ala Met Leu Leu Leu Leu Thr	
	15 20 25 30	
	ctt gcc ctc ctg ggg ggc ccc acc tgg gca ggg aag atg tat ggc cct	145
	Leu Ala Leu Leu Gly Gly Pro Thr Trp Ala Gly Lys Met Tyr Gly Pro	
10	35 40 45	
	gga gga ggc aag tat ttc agc acc act gaa gac tac gac cat gaa atc	193
	Gly Gly Gly Lys Tyr Phe Ser Thr Thr Glu Asp Tyr Asp His Glu Ile	
	50 55 60	
	aca ggg ctg cgg gtg tct gta ggt ctt ctc ctg gtg aaa agt gtc cag	241
15	Thr Gly Leu Arg Val Ser Val Gly Leu Leu Leu Val Lys Ser Val Gln	
	65 70 75	
	gtg aaa ctt gga gac tcc tgg gac gtg aaa ctg gga gcc tta ggt ggg	289
	Val Lys Leu Gly Asp Ser Trp Asp Val Lys Leu Gly Ala Leu Gly Gly	
	80 85 90	
20	aat acc cag gaa gtc acc ctg cag cca ggc gaa tac atc aca aaa gtc	337
	Asn Thr Gln Glu Val Thr Leu Gln Pro Gly Glu Tyr Ile Thr Lys Val	
	95 100 105 110	
	ttt gtc gcc ttc caa gct ttc ctc cgg ggt atg gtc atg tac acc agc	385
	Phe Val Ala Phe Gln Ala Phe Leu Arg Gly Met Val Met Tyr Thr Ser	
25	115 120 125	
	aag gac cgc tat ttc tat ttt ggg aag ctt gat ggc cag atc tcc tct	433
	Lys Asp Arg Tyr Phe Tyr Phe Gly Lys Leu Asp Gly Gln Ile Ser Ser	
	130 135 140	
	gcc tac ccc agc caa gag ggg cag gtg ctg gtg ggc atc tat ggc cag	481
30	Ala Tyr Pro Ser Gln Glu Gly Gln Val Leu Val Gly Ile Tyr Gly Gln	
	145 150 155	
	tat caa ctc ctt ggc atc aag agc att ggc ttt gaa tgg aat tat cca	529
	Tyr Gln Leu Leu Gly Ile Lys Ser Ile Gly Phe Glu Trp Asn Tyr Pro	
	160 165 170	
35	cta gag gag ccg acc act gag cca cca gtt aat ctc aca tac tca gca	577

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	255	260	265	
	gcc aaa gtt ctg aag aca gtg act ttt gca aat gat cta aaa cca aag			926
	Ala Lys Val Leu Lys Thr Val Thr Phe Ala Asn Asp Leu Lys Pro Lys			
	270	275	280	
5	gtg tat aat cta aag aag gac ttt tcc cgt tta gaa cca tta gta aat			974
	Val Tyr Asn Leu Lys Lys Asp Phe Ser Arg Leu Glu Pro Leu Val Asn			
	285	290	295	
	gat tta aca cta cgc att ggg aga ttg gtt acc gac tta cta caa aga			1022
	Asp Leu Thr Leu Arg Ile Gly Arg Leu Val Thr Asp Leu Leu Gln Arg			
10	300	305	310	315
	gag aaa gaa att gct ttc tta agt gaa aaa ata tct aat tta aca ata			1070
	Glu Lys Glu Ile Ala Phe Leu Ser Glu Lys Ile Ser Asn Leu Thr Ile			
	320	325	330	
	gtc caa gct gag att aag gat att aaa gat gaa ata gca cac att tca			1118
15	Val Gln Ala Glu Ile Lys Asp Ile Lys Asp Glu Ile Ala His Ile Ser			
	335	340	345	
	gat atg aat tagtttgaca ttattgagat tagactaagg taattttttt aat			1170
	Asp Met Asn			
	350			
20	gggacctctc atgagaagac tggtaaataca aaaataatga tatttttgag caaaagtcac			1230
	tttatatttta atcctatttt gtacagtaaa aataaaactt taaaacaggt tgattttcca			1290
	aaataaatat gctaaaacct			1310
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	<213> Homo Sapience			
	<220>			
	<221> CDS			
30	<222> (233)...(556)			
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	tgtcagccgc ccccccccc ccatatgcag atttactogg catggtagtg gccagcttct			120
35	aacacagctg gtatttcaag tctcctggga cctcactcag gaatgatacc ccctcagtag			180

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	aagcagcagg tgatcttaac tcctttcaaa gagcaggect gtctgggaag cc atg	235
	Met	
	1	
	tcc tca gca ggc aca gca acc cct ctg gaa atg gat cac aaa ctc act	283
5	Ser Ser Ala Gly Thr Ala Thr Pro Leu Glu Met Asp His Lys Leu Thr	
	5 10 15	
	tct cag cca ggc agg cca agc ttc tat tgt aac agt agg cac agt ata	331
	Ser Gln Pro Gly Arg Pro Ser Phe Tyr Cys Asn Ser Arg His Ser Ile	
	20 25 30	
10	gtc gga tca tca cat cag ctg ggt ttt tgg ttt agt cat cta gag tcg	379
	Val Gly Ser Ser His Gln Leu Gly Phe Trp Phe Ser His Leu Glu Ser	
	35 40 45	
	tct gga cta aag gtc ttt cag gtc tcc ttg ccc tgt gag tgc gtg aac	427
	Ser Gly Leu Lys Val Phe Gln Val Ser Leu Pro Cys Glu Cys Val Asn	
15	50 55 60 65	
	ctc ccc acc cga att gcc tca gtt gtc ctg agc ctc atg tct ctc ctg	475
	Leu Pro Thr Arg Ile Ala Ser Val Val Leu Ser Leu Met Ser Leu Leu	
	70 75 80	
	gtg gtg ggc cag gcc cct gca tgg gaa ggg agc ctg ctg cgg ggc agg	523
20	Val Val Gly Gln Ala Pro Ala Trp Glu Gly Ser Leu Leu Arg Gly Arg	
	85 90 95	
	cca gct ggg ggt gct cac cta tgc gca gca tgaagttatt gaaggac	570
	Pro Ala Gly Gly Ala His Leu Cys Ala Ala	
	100 105	
25	tggttggtga tggttggtgag cgtatccttc atggccagcg cgaagtcggc caggtcagcc	630
	aggtgctgcc agcgtctctc ctcggacttg tcttcctgtg ccaggggacc gtggagaaag	690
	tgtcaggggc cgctcactgc agcagcctgc tctgctgeet tcctggcag tgttctgggg	750
	gtggattccc tacacctaga tgttcaaggc cttacttttc ctcccacaaa ggagtcgcag	810
	ccacgctagc tctgacttgc cactgtgaca aagttcacgt agcaggtcta ggcaaagact	870
30	gggcaattga gcagaggaga cggacctgtg agtctgacca cgaggcggac cccttcacct	930
	tggttgggac tggctcctggt ccttaggttt tgctcaggttgc tcttctgttg gatccctcaa	990
	ctaggtgata agcaactggag ggggatgacc cgccttggac gtgtttcttt aacctcatcc	1050
	atataatagg gccgtgggat ggtttagtag gtaaagcagg atgatggtgt tttaagacca	1110
	gagcttgga ccagggtcc tacacctaat tttctctcct ggtagctgaa caaaggtcta	1170
35	aattagctta acaaaagaac aggtgcctc cagccagagt tctgaaggcc atgctttcag	1230

10	<400>	121
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	1 5 10 15	
	Val Ser Glu Ala Lys Phe Asp Asp Phe Glu Asp Glu Glu Asp Ile Val	
	20 25 30	
15	Glu Tyr Asp Asp Asn Asp Phe Ala Glu Phe Glu Asp Val Met Glu Asp	
	35 40 45	
	Ser Val Thr Glu Ser Pro Gln Arg Val Ile Ile Thr Glu Asp Asp Glu	
	50 55 60	
	Asp Glu Thr Thr Val Glu Leu Glu Gly Gln Asp Glu Asn Gln Glu Gly	
20	65 70 75 80	
	Asp Phe Glu Asp Ala Asp Thr Gln Glu Gly Asp Thr Glu Ser Glu Pro	
	85 90 95	
	Tyr Asp Asp Glu Glu Phe Glu Gly Tyr Glu Asp Lys Pro Asp Thr Ser	
	100 105 110	
25	Ser Ser Lys Asn Lys Asp Pro Ile Thr Ile Val Asp Val Pro Ala His	
	115 120 125	
	Leu Gln Asn Ser Trp Glu Ser Tyr Tyr Leu Glu Ile Leu Met Val Thr	
	130 135 140	
	Gly Leu Leu Ala Tyr Ile Met Asn Tyr Ile Ile Gly Lys Asn Lys Asn	
30	145 150 155 160	
	Ser Arg Leu Ala Gln Ala Trp Phe Asn Thr His Arg Glu Leu Leu Glu	
	165 170 175	
	Ser Asn Phe Thr Leu Val Gly Asp Asp Gly Thr Asn Lys Glu Ala Thr	
	180 185 190	
35	Ser Thr Gly Lys Leu Asn Gln Glu Asn Glu His Ile Tyr Asn Leu Trp	

	195	200	205
	Cys Ser Gly Arg Val Cys Cys Glu Gly Met Leu Ile Gln Leu Arg Phe		
	210	215	220
5	Leu Lys Arg Gln Asp Leu Leu Asn Val Leu Ala Arg Met Met Arg Pro		
	225	230	235 240
	Val Ser Asp Gln Val Gln Ile Lys Val Thr Met Asn Asp Glu Asp Met		
	245	250	255
	Asp Thr Tyr Val Phe Ala Val Gly Thr Arg Lys Ala Leu Val Arg Leu		
	260	265	270
10	Gln Lys Glu Met Gln Asp Leu Ser Glu Phe Cys Ser Asp Lys Pro Lys		
	275	280	285
	Ser Gly Ala Lys Tyr Gly Leu Pro Asp Ser Leu Ala Ile Leu Ser Glu		
	290	295	300
	Met Gly Glu Val Thr Asp Gly Met Met Asp Thr Lys Met Val His Phe		
15	305	310	315 320
	Leu Thr His Tyr Ala Asp Lys Ile Glu Ser Val His Phe Ser Asp Gln		
	325	330	335
	Phe Ser Gly Pro Lys Ile Met Gln Glu Glu Gly Gln Pro Leu Lys Leu		
	340	345	350
20	Pro Asp Thr Lys Arg Thr Leu Leu Phe Thr Phe Asn Val Pro Gly Ser		
	355	360	365
	Gly Asn Thr Tyr Pro Lys Asp Met Glu Ala Leu Leu Pro Leu Met Asn		
	370	375	380
	Met Val Ile Tyr Ser Ile Asp Lys Ala Lys Lys Phe Arg Leu Asn Arg		
25	385	390	395 400
	Glu Gly Lys Gln Lys Ala Asp Lys Asn Arg Ala Arg Val Glu Glu Asn		
	405	410	415
	Phe Leu Lys Leu Thr His Val Gln Arg Gln Glu Ala Ala Gln Ser Arg		
	420	425	430
30	Arg Glu Glu Lys Lys Arg Ala Glu Lys Glu Arg Ile Met Asn Glu Glu		
	435	440	445
	Asp Pro Glu Lys Gln Arg Arg Leu Glu Glu Ala Ala Leu Arg Arg Glu		
	450	455	460
	Gln Lys Lys Leu Glu Lys Lys Gln Met Lys Met Lys Gln Ile Lys Val		
35	465	470	475 480

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Lys Ala Met

<210> 122

<211> 334

5 <212> PRT

<213> Homo sapience

<400> 122

10 Met Val Glu Phe Ala Pro Leu Phe Met Pro Trp Glu Arg Arg Leu Gln
 1 5 10 15
 Thr Leu Ala Val Leu Gln Phe Val Phe Ser Phe Leu Ala Leu Ala Glu
 20 25 30
 Ile Cys Thr Val Gly Phe Ile Ala Leu Leu Phe Thr Arg Phe Trp Leu
 35 40 45
 15 Leu Thr Val Leu Tyr Ala Ala Trp Trp Tyr Leu Asp Arg Asp Lys Pro
 50 55 60
 Arg Gln Gly Gly Arg His Ile Gln Ala Ile Arg Cys Trp Thr Ile Trp
 65 70 75 80
 Lys Tyr Met Lys Asp Tyr Phe Pro Ile Ser Leu Val Lys Thr Ala Glu
 20 85 90 95
 Leu Asp Pro Ser Arg Asn Tyr Ile Ala Gly Phe His Pro His Gly Val
 100 105 110
 Leu Ala Val Gly Ala Phe Ala Asn Leu Cys Thr Glu Ser Thr Gly Phe
 115 120 125
 25 Ser Ser Ile Phe Pro Gly Ile Arg Pro His Leu Met Met Leu Thr Leu
 130 135 140
 Trp Phe Arg Ala Pro Phe Phe Arg Asp Tyr Ile Met Ser Ala Gly Leu
 145 150 155 160
 Val Thr Ser Glu Lys Glu Ser Ala Ala His Ile Leu Asn Arg Lys Gly
 30 165 170 175
 Gly Gly Asn Leu Leu Gly Ile Ile Val Gly Gly Ala Gln Glu Ala Leu
 180 185 190
 Asp Ala Arg Pro Gly Ser Phe Thr Leu Leu Leu Arg Asn Arg Lys Gly
 195 200 205
 35 Phe Val Arg Leu Ala Leu Thr His Gly Ala Pro Leu Val Pro Ile Phe

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210 215 220
 Ser Phe Gly Glu Asn Asp Leu Phe Asp Gln Ile Pro Asn Ser Ser Gly
 225 230 235 240
 Ser Trp Leu Arg Tyr Ile Gln Asn Arg Leu Gln Lys Ile Met Gly Ile
 5 245 250 255
 Ser Leu Pro Leu Phe His Gly Arg Gly Val Phe Gln Tyr Ser Phe Gly
 260 265 270
 Leu Ile Pro Tyr Arg Arg Pro Ile Thr Thr Val Val Gly Lys Pro Ile
 275 280 285
 10 Glu Val Gln Lys Thr Leu His Pro Ser Glu Glu Glu Val Asn Gln Leu
 290 295 300
 His Gln Arg Tyr Ile Lys Glu Leu Cys Asn Leu Phe Glu Ala His Lys
 305 310 315 320
 Leu Lys Phe Asn Ile Pro Ala Asp Gln His Leu Glu Phe Cys
 15 325 330

 <210> 123
 <211> 267
 <212> PRT
 20 <213> Homo sapience

 <400> 123
 Met Ala Pro Trp Ala Leu Leu Ser Pro Gly Val Leu Val Arg Thr Gly
 1 5 10 15
 25 His Thr Val Leu Thr Trp Gly Ile Thr Leu Val Leu Phe Leu His Asp
 20 25 30
 Thr Glu Leu Arg Gln Trp Glu Glu Gln Gly Glu Leu Leu Leu Pro Leu
 35 40 45
 Thr Phe Leu Leu Leu Val Leu Gly Ser Leu Leu Leu Tyr Leu Ala Val
 30 50 55 60
 Ser Leu Met Asp Pro Gly Tyr Val Asn Val Gln Pro Gln Pro Gln Glu
 65 70 75 80
 Glu Leu Lys Glu Glu Gln Thr Ala Met Val Pro Pro Ala Ile Pro Leu
 85 90 95
 35 Arg Arg Cys Arg Tyr Cys Leu Val Leu Gln Pro Leu Arg Ala Arg His

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	100	105	110
	Cys Arg Glu Cys Arg Arg Cys Val Arg Arg Tyr Asp His His Cys Pro		
	115	120	125
	Trp Met Glu Asn Cys Val Gly Glu Arg Asn His Pro Leu Phe Val Val		
5	130	135	140
	Tyr Leu Ala Leu Gln Leu Val Val Leu Leu Trp Gly Leu Tyr Leu Ala		
	145	150	155
	Trp Ser Gly Leu Arg Phe Phe Gln Pro Trp Gly Leu Trp Leu Arg Ser		
	165	170	175
10	Ser Gly Leu Leu Phe Ala Thr Phe Leu Leu Leu Ser Leu Phe Ser Leu		
	180	185	190
	Val Ala Ser Leu Leu Leu Val Ser His Leu Tyr Leu Val Ala Ser Asn		
	195	200	205
	Thr Thr Thr Trp Glu Phe Ile Ser Ser His Arg Ile Ala Tyr Leu Arg		
15	210	215	220
	Gln Arg Pro Ser Asn Pro Phe Asp Arg Gly Leu Thr Arg Asn Leu Ala		
	225	230	235
	His Phe Phe Cys Gly Trp Pro Ser Gly Ser Trp Glu Thr Leu Trp Ala		
	245	250	255
20	Glu Glu Glu Glu Glu Gly Ser Ser Pro Ala Val		
	260	265	

<210> 124

<211> 106

25 <212> PRT

<213> Homo sapience

<400> 124

	Met Ser Thr Asn Asn Met Ser Asp Pro Arg Arg Pro Asn Lys Val Leu
30	1 5 10 15
	Arg Tyr Lys Pro Pro Pro Ser Glu Cys Asn Pro Ala Leu Asp Asp Pro
	20 25 30
	Thr Pro Asp Tyr Met Asn Leu Leu Gly Met Ile Phe Ser Met Cys Gly
	35 40 45
35	Leu Met Leu Lys Leu Lys Trp Cys Ala Trp Val Ala Val Tyr Cys Ser

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50 55 60
 Phe Ile Ser Phe Ala Asn Ser Arg Ser Ser Glu Asp Thr Lys Gln Met
 65 70 75 80
 Met Ser Ser Phe Met Leu Ser Ile Ser Ala Val Val Met Ser Tyr Leu
 5 85 90 95
 Gln Asn Pro Gln Pro Met Thr Pro Pro Trp
 100 105

 <210> 125
 10 <211> 224
 <212> PRT
 <213> Homo sapience

 <400> 125
 15 Met Thr Leu Phe His Phe Gly Asn Cys Phe Ala Leu Ala Tyr Phe Pro
 1 5 10 15
 Tyr Phe Ile Thr Tyr Lys Cys Ser Gly Leu Ser Glu Tyr Asn Ala Phe
 20 25 30
 Trp Lys Cys Val Gln Ala Gly Val Thr Tyr Leu Phe Val Gln Leu Cys
 20 35 40 45
 Lys Met Leu Phe Leu Ala Thr Phe Phe Pro Thr Trp Glu Gly Gly Ile
 50 55 60
 Tyr Asp Phe Ile Gly Glu Phe Met Lys Ala Ser Val Asp Val Ala Asp
 65 70 75 80
 25 Leu Ile Gly Leu Asn Leu Val Met Ser Arg Asn Ala Gly Lys Gly Glu
 85 90 95
 Tyr Lys Ile Met Val Ala Ala Leu Gly Trp Ala Thr Ala Glu Leu Ile
 100 105 110
 Met Ser Arg Cys Ile Pro Leu Trp Val Gly Ala Arg Gly Ile Glu Phe
 30 115 120 125
 Asp Trp Lys Tyr Ile Gln Met Ser Ile Asp Ser Asn Ile Ser Leu Val
 130 135 140
 His Tyr Ile Val Ala Ser Ala Gln Val Trp Met Ile Thr Arg Tyr Asp
 145 150 155 160
 35 Leu Tyr His Thr Phe Arg Pro Ala Val Leu Leu Leu Met Phe Leu Ser

[illegible]

35 <210> 128

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<211> 91

<212> PRT

<213> Homo sapience

5 <400> 128

Met Val Tyr Ile Ser Asn Gly Gln Val Leu Asp Ser Arg Ser Gln Ser

1 5 10 15

Pro Trp Arg Leu Ser Leu Ile Thr Asp Phe Phe Trp Gly Ile Ala Glu

20 25 30

10 Phe Val Val Leu Phe Phe Lys Thr Leu Leu Gln Gln Asp Val Lys Lys

35 40 45

Arg Arg Ser Tyr Gly Asn Ser Ser Asp Ser Arg Tyr Asp Asp Gly Arg

50 55 60

Gly Pro Pro Gly Asn Pro Pro Arg Arg Met Gly Arg Ile Asn His Leu

15 65 70 75 80

Arg Gly Pro Ser Pro Pro Met Ala Gly Gly

85 90

<210> 129

20 <211> 344

<212> PRT

<213> Homo sapience

<400> 129

25 Met Phe Thr Ser Thr Gly Ser Ser Gly Leu Tyr Lys Ala Pro Leu Ser

1 5 10 15

Lys Ser Leu Leu Leu Val Pro Ser Ala Leu Ser Leu Leu Ala Leu

20 25 30

Leu Leu Pro His Cys Gln Lys Leu Phe Val Tyr Asp Leu His Ala Val

30 35 40 45

Lys Asn Asp Phe Gln Ile Trp Arg Leu Ile Cys Gly Arg Ile Ile Cys

50 55 60

Leu Asp Leu Lys Asp Thr Phe Cys Ser Ser Leu Leu Ile Tyr Asn Phe

65 70 75 80

35 Arg Ile Phe Glu Arg Arg Tyr Gly Ser Arg Lys Phe Ala Ser Phe Leu

[illegible]

35 225 230 235 240

	Ser Arg Lys Gln Arg Gln Leu Lys Ala Asp Ala Lys Lys Lys Ala Ile Gly	
	245	250 255
	Arg Leu Gln Leu Arg Thr Leu Lys Gln Gly Asp Lys Glu Ile Gly Pro	
	260	265 270
5	Asp Gly Asp Ser Cys Ala Val Cys Ile Glu Leu Tyr Lys Pro Asn Asp	
	275	280 285
	Leu Val Arg Ile Leu Thr Cys Asn His Ile Phe His Lys Thr Cys Val	
	290	295 300
	Asp Pro Trp Leu Leu Glu His Arg Thr Cys Pro Met Cys Lys Cys Asp	
10	305	310 315 320
	Ile Leu Lys Ala Leu Gly Ile Glu Val Asp Val Glu Asp Gly Ser Val	
	325	330 335
	Ser Leu Gln Val Pro Val Ser Asn Glu Ile Ser Asn Ser Ala Ser Ser	
	340	345 350
15	His Glu Glu Asp Asn Arg Ser Glu Thr Ala Ser Ser Gly Tyr Ala Ser	
	355	360 365
	Val Gln Gly Thr Asp Glu Pro Pro Leu Glu Glu His Val Gln Ser Thr	
	370	375 380
	Asn Glu Ser Leu Gln Leu Val Asn His Glu Ala Asn Ser Val Ala Val	
20	385	390 395 400
	Asp Val Ile Pro His Val Asp Asn Pro Thr Phe Glu Glu Asp Glu Thr	
	405	410 415
	Pro Asn Gln Glu Thr Ala Val Arg Glu Ile Lys Ser	
	420	425
25	<210> 131	
	<211> 1449	
	<212> DNA	
	<213> Homo sapience	
30	<400> 131	
	atgaaagcct tccacacttt ctgtgttgtc cttctggtgt ttgggagtgt ctctgaagcc	60
	aagtttgatg attttgagga tgaggaggac atagtagagt atgatgataa tgacttcgct	120
	gaatttgagg atgtcatgga agactctgtt actgaatctc ctcaacgggt cataatcact	180
35	gaagatgatg aagatgagac cactgtggag ttggaagggc aggatgaaaa ccaagaagga	240

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gattttgaag atgcagatac ccaggaggga gatactgaga gtgaaccata tgatgatgaa 300
gaatttgaag gttatgaaga caaaccagat acttcttcta gcaaaaataa agaccaata 360
acgattgttg atgttcctgc acacctccag aacagctggg agagttatta tctagaaatt 420
ttgatggtga ctggtctget tgcttatatc atgaattaca tcattgggaa gaataaaaac 480
5 agtcgccttg cacaggcctg gtttaacact catagggagc ttttggagag caactttact 540
ttagtggggg atgatggaac taacaaagaa gccacaagca caggaaagtt gaaccaggag 600
aatgagcaca tctataacct gtggtgttct ggtcgagtgt gctgtgaggg catgettatc 660
cagctgaggt tcctcaagag acaagactta ctgaatgtcc tggcccggat gatgaggcca 720
gtgagtgate aagtgc aaat aaaagtaacc atgaatgatg aagacatgga tacctacgta 780
10 tttgctgttg gcacacggaa agccttggtg cgactacaga aagagatgca ggatttgagt 840
gagttttgta gtgataaacc taagtctgga gcaaagtatg gactgccgga ctctttggcc 900
atcctgtcag agatgggaga agtcacagac ggaatgatgg atacaaagat ggttcacttt 960
cttacacact atgctgacaa gattgaatct gttcattttt cagaccagtt ctctgggtcca 1020
aaaattatgc aagaggaagg tcagccttta aagctacctg aactaagag gacactgttg 1080
15 tttacattta atgtgcctgg ctacaggaac acttacccaa aggatatgga ggcactgeta 1140
cccctgatga acatggtgat ttattctatt gataaaagcca aaaagttccg actcaacaga 1200
gaaggcaaac aaaaagcaga taagaacctg gcccgagtag aagagaactt cttgaaactg 1260
acacatgtgc aaagacagga agcagcacag tctcgccggg aggagaaaaa aagagcagag 1320
aaggagcgaa tcattgaatga ggaagatcct gagaaacagc gcaggctgga ggaggctgca 1380
20 ttgaggcgtg agcaaaagaa gttggaaaag aagcaaatga aatgaaaca aatcaaagtg 1440
aaagccatg 1449

<210> 132

<211> 1002

25 <212> DNA

<213> Homo sapience

<400> 132

atggtagagt tcgcgcctt gtttatgccg tgggagcgca ggctgcagac acttgctgtc 60
30 ctacagtttg tcttctcctt cttggcactg gccgagatct gcaactgtggg cttcatagcc 120
ctcctgttta caagattctg gtcctcact gtcctgtatg cggcctggtg gtatctggac 180
cgagacaagc cacggcaggg gggcgggcac atccaggcca tcagggtctg gactatatgg 240
aagtacatga aggactatct ccccatctcg ctggtoaaga ctgctgagct ggacccctct 300
cggaactaca ttgcgggctt cccccccat ggagtcctgg cagtcggagc ctttgccaac 360
35 ctgtgcactg agagcacagg cttctcttcg atcttccccg gtatccgccc ccatctgatg 420

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atgctgacct tgtggttcgg ggccecttc ttccagagatt acatcatgtc tgcagggttg 480
gtcacatcag aaaaggagag tgctgtctac attctgaaca ggaagggtgg cggaaacttg 540
ctgggcatca ttgtaggggg tgcccaggag gccctggatg ccaggcctgg atccttcacg 600
ctgttactgc ggaaccgaaa gggttcgtc aggtctgccc tgacacacgg ggcacccctg 660
5 gtgccaatct tctccttcgg ggagaatgac ctatttgacc agattcccaa ctcttctggc 720
tcctgggttac gctatatcca gaatcggttg cagaagatca tgggcatctc cctcccaactc 780
tttcatggcc gtggtgtctt ccagtacagc tttggtttaa taccctaccg ccggcccatc 840
accactgtgg tggggaagcc catcgaggta cagaagacgc tgcacccctc ggaggaggag 900
gtgaaccagc tgcaccagcg ttatatcaaa gagctgtgca acctcttcga ggcccacaaa 960
10 cttagttca acatccctgc tgaccagcac ttggagttct gc 1002

<210> 133

<211> 801

<212> DNA

15 <213> Homo sapience

<400> 133

atggcgccct gggcgctcct cagccctggg gtccctggtg ggaccgggca caccgtgctg 60
acctggggaa tcacgtggtg gctcttctcg caccataccg agctgcggca atgggaggag 120
20 cagggggagc tgctcctgcc cctcaccttc ctgctcctgg tgctgggctc cctgctgctc 180
tacctcgctg tgtaactcat ggaccctggc tacgtgaatg tgcagcccca gcctcaggag 240
gagctcaaag aggagcagac agccatggtt cctccagcca tccctcttcg gcgctgcaga 300
tactgcctgg tgctgcagcc cctgagggtt cggcactgcc gtgagtgcg ccgttgcgctc 360
cgccgctacg accaccactg cccctggatg gagaactgtg tgggagagcg caaccaccca 420
25 ctctttgtgg tctacctggc gctgcagctg gtggtgcttc tgtggggcct gtacctggca 480
tggtcaggcc tccggttctt ccagccctgg ggtctgtggt tgcgggtccag cgggctcctg 540
ttcgccacct tcctgctgct gtccctcttc tcgttggtgg ccagcctgct cctcgtctcg 600
cacctctacc tgggtggccag caacaccacc acctgggaat tcatctctc acaccgcatac 660
gcctatctcc gccagcgccc cagcaacccc ttcgaccgag gcctgacccg caacctggcc 720
30 cacttcttct gtggatggcc ctcagggtcc tgggagaccc tctgggctga ggaggaggaa 780
gagggcagca gccagctgt t 801

<210> 134

<211> 318

35 <212> DNA

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<213> Homo sapience

<400> 134

	atgtccacta acaatatgtc ggacccacgg aggccgaaca aagtgtctgag gtacaagccc	60
5	ccgccgagcg aatgtaaccc ggcccttgac gaccgcagcg cggactacat gaacctgtctg	120
	ggcatgatct tcagcatgtg cggcctcatg cttaagctga agtgggtgtgc ttgggtcgtct	180
	gtctactgtc ccttcacacg ctttgccaac tctcggagct cggaggacac gaagcaaatg	240
	atgagtagct tcatgtgtgc catctctgcc gtgggtgatgt cctatctgca gaatectcag	300
	cccatgacgc ccccatgg	318

10

<210> 135

<211> 672

<212> DNA

<213> Homo sapience

15

<400> 135

	atgacctgt ttcaacttgg gaactgtctc gctcttgcct acttccccta cttcaccacc	60
	tacaagtga gcggcctgtc cgagtacaac gccttctgga aatgcgtcca ggcctggagtc	120
	acctacctct ttgtccaact ctgcaagatg ctgttcttgg ccactttctt tcccacctgg	180
20	gaaggcggca tetatgactt cattggggag ttcatgaagg ccagcgtgga tgtggcagac	240
	ctgataggtc taaaccttgt catgtcccgg aatgccggca agggagagta caagatcatg	300
	gttgcctgcc tgggctgggc cactgctgag cttattatgt cccgctgcat tcccctatgg	360
	gtcggagccc ggggcattga gtttgactgg aagtacatcc agatgagcat agactccaac	420
	atcagtctgg tccattacat cgctcgtctc gctcaggtct ggatgataac acgetatgat	480
25	ctgtaccaca ccttcgggcc agctgtcttc ctgctgatgt tctcagtgct ctacaaggcc	540
	tttgttatgg agaccttcgt ccacctctgc tcgctgggca gttgggcagc tctactggcc	600
	cgagcagtg taacggggct gctggccctc agcacttttg ccctgtatgt cgcgcttgct	660
	aatgtgcaact cc	672

30

<210> 136

<211> 774

<212> DNA

<213> Homo sapience

35

<400> 136

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	atggcgggtct tggcacctct aattgtctct gtgtattcgg tgccgcgact ttcacgatgg	60
	ctcgcccaac cttactacct tctgtcggcc ctgctctctg ctgccttctt actcgtgagg	120
	aaactgccgc cgctctgcc a cggctctgcc acccaacgcg aagacggtaa cccgtgtgac	180
	tttgactgga gagaagtga gatcctgatg tttctcagtg ccattgtgat gatgaagaac	240
5	cgcagatcca tgttcctgat gacgtgcaaa cccccctat atatgggccc tgagtatac	300
	aagtacttca atgataaaac cattgatgag gaactagaac gggacaagag ggtcacttgg	360
	attgtggagt tctttgccaa ttggtotaat gactgccaat catttgcccc tatctatgct	420
	gaactctccc ttaaatacaa ctgtacaggg ctaaattttg ggaagggtga tgttggaagc	480
	tatactgatg ttagtacgcg gtacaaagtg agcacatcac ccctcaccaa gcaactccct	540
10	accctgatcc tgttccaagg tggcaaggag gcaatgcggc ggccacagat tgacaagaaa	600
	ggacgggctg tctcatggac cttctctgag gagaatgtga tccgagaatt taacttaaat	660
	gagctatacc agcgggccaa gaaactatca aagcgtggag acaatatccc tgaggagcag	720
	cctgtggctt caacccccac cacagtgtca gatggggaaa acaagaagga taaa	774
15	<210> 137	
	<211> 330	
	<212> DNA	
	<213> Homo sapience	
20	<400> 137	
	atggcgcggg tgggtggcaa gcgggaaggg ccgcggttca tcagcgaggc ggccgtgcgg	60
	ggcaacgcgc ccgtcctgga ttattgcgg accctcgggtg cagcgtgtgc gggggccacg	120
	gccggcatcc tggcctcac cggcctctac ggcttcatct tctacctgct cgcctccgct	180
	ctgctctccc tgctcctcat tctcaaggcg ggaaggaggt ggaacaaata tttcaaatca	240
25	cggagacctc tctttacagg aggcctcatc gggggcctct tcacctacgt cctgttctgg	300
	acgttctctt acggcatggt gcacgtctac	330
	<210> 138	
	<211> 273	
30	<212> DNA	
	<213> Homo sapience	
	<400> 138	
	atggtttaca tctcgaacgg acaagtgttg gacagccgga gtcagtctcc atggagatta	60
35	tctttgataa cagatttctt ctgggggaata gctgagtttg tggttttgtt tttcaaaact	120

35 <400> 140

35 a atg aaa gcc ttc cac act ttc tgt gtt gtc ctt ctg gtg ttt ggg 166

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Met Lys Ala Phe His Thr Phe Cys Val Val Leu Leu Val Phe Gly

	1	5	10	15	
	agt gtc tct gaa gcc aag ttt gat gat ttt gag gat gag gag gac ata	214			
	Ser Val Ser Glu Ala Lys Phe Asp Asp Phe Glu Asp Glu Glu Asp Ile				
5		20	25	30	
	gta gag tat gat gat aat gac ttc gct gaa ttt gag gat gtc atg gaa	262			
	Val Glu Tyr Asp Asp Asn Asp Phe Ala Glu Phe Glu Asp Val Met Glu				
	35	40	45		
	gac tct gtt act gaa tct cct caa cgg gtc ata atc act gaa gat gat	310			
10	Asp Ser Val Thr Glu Ser Pro Gln Arg Val Ile Ile Thr Glu Asp Asp				
	50	55	60		
	gaa gat gag acc act gtg gag ttg gaa ggg cag gat gaa aac caa gaa	358			
	Glu Asp Glu Thr Thr Val Glu Leu Glu Gly Gln Asp Glu Asn Gln Glu				
	65	70	75		
15	gga gat ttt gaa gat gca gat acc cag gag gga gat act gag agt gaa	406			
	Gly Asp Phe Glu Asp Ala Asp Thr Gln Glu Gly Asp Thr Glu Ser Glu				
	80	85	90	95	
	cca tat gat gat gaa gaa ttt gaa ggt tat gaa gac aaa cca gat act	454			
	Pro Tyr Asp Asp Glu Glu Phe Glu Gly Tyr Glu Asp Lys Pro Asp Thr				
20		100	105	110	
	tct tct agc aaa aat aaa gac cca ata acg att gtt gat gtt cct gca	502			
	Ser Ser Ser Lys Asn Lys Asp Pro Ile Thr Ile Val Asp Val Pro Ala				
	115	120	125		
	cac ctc cag aac agc tgg gag agt tat tat cta gaa att ttg atg gtg	550			
25	His Leu Gln Asn Ser Trp Glu Ser Tyr Tyr Leu Glu Ile Leu Met Val				
	130	135	140		
	act ggt ctg ctt gct tat atc atg aat tac atc att ggg aag aat aaa	598			
	Thr Gly Leu Leu Ala Tyr Ile Met Asn Tyr Ile Ile Gly Lys Asn Lys				
	145	150	155		
30	aac agt cgc ctt gca cag gcc tgg ttt aac act cat agg gag ctt ttg	646			
	Asn Ser Arg Leu Ala Gln Ala Trp Phe Asn Thr His Arg Glu Leu Leu				
	160	165	170	175	
	gag agc aac ttt act tta gtg ggg gat gat gga act aac aaa gaa gcc	694			
	Glu Ser Asn Phe Thr Leu Val Gly Asp Asp Gly Thr Asn Lys Glu Ala				
35		180	185	190	

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	370	375	380	
	aac atg gtg att tat tct att gat aaa gcc aaa aag ttc cga ctc aac			1318
	Asn Met Val Ile Tyr Ser Ile Asp Lys Ala Lys Lys Phe Arg Leu Asn			
	385	390	395	
5	aga gaa ggc aaa caa aaa gca gat aag aac cgt gcc cga gta gaa gag			1366
	Arg Glu Gly Lys Gln Lys Ala Asp Lys Asn Arg Ala Arg Val Glu Glu			
	400	405	410	415
	aac ttc ttg aaa ctg aca cat gtg caa aga cag gaa gca gca cag tct			1414
	Asn Phe Leu Lys Leu Thr His Val Gln Arg Gln Glu Ala Ala Gln Ser			
10	420	425	430	
	cgg cgg gag gag aaa aaa aga gca gag aag gag cga atc atg aat gag			1462
	Arg Arg Glu Glu Lys Lys Arg Ala Glu Lys Glu Arg Ile Met Asn Glu			
	435	440	445	
	gaa gat cct gag aaa cag cgc agg ctg gag gag gct gca ttg agg cgt			1510
15	Glu Asp Pro Glu Lys Gln Arg Arg Leu Glu Glu Ala Ala Leu Arg Arg			
	450	455	460	
	gag caa aag aag ttg gaa aag aag caa atg aaa atg aaa caa atc aaa			1558
	Glu Gln Lys Lys Leu Glu Lys Lys Gln Met Lys Met Lys Gln Ile Lys			
	465	470	475	
20	gtg aaa gcc atg taaagccatc ccagagattt gagttctgat gccacctgta			1610
	Val Lys Ala Met			
	480			
	agctctgaat tcacaggaaa catgaaaaac gccagtccat ttctcaacct taaatttcag			1670
	acagtcttgg gcaactgaga aatcettatt tcatcatcta ctctgtttgg ggtttgggt			1730
25	tttacagaga ttgaagatac ctggaaaggg ctctgtttca agaatttttt ttccagata			1790
	atcaaattat tttgattatt ttataaaagg aatgatctat gaaatctgtg taggttttaa			1850
	atattttaaa aattataata caaatcatca gtgcttttag tacttcagtg tttaaagaaa			1910
	taccatgaaa tttataggta gataaccaga ttgttgcttt ttgtttaaac caagcagttg			1970
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35 Leu Thr Leu Trp Phe Arg Ala Pro Phe Phe Arg Asp Tyr Ile Met Ser

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	145	150	155	
	gca ggg ttg gtc aca tca gaa aag gag agt gct gct cac att ctg aac			588
	Ala Gly Leu Val Thr Ser Glu Lys Glu Ser Ala Ala His Ile Leu Asn			
	160	165	170	
5	agg aag ggt ggc gga aac ttg ctg ggc atc att gta ggg ggt gcc cag			636
	Arg Lys Gly Gly Gly Asn Leu Leu Gly Ile Ile Val Gly Gly Ala Gln			
	175	180	185	
	gag gcc ctg gat gcc agg cct gga tcc ttc acg ctg tta ctg cgg aac			684
	Glu Ala Leu Asp Ala Arg Pro Gly Ser Phe Thr Leu Leu Leu Arg Asn			
10	190	195	200	205
	cga aag ggc ttc gtc agg ctc gcc ctg aca cac ggg gca ccc ctg gtg			732
	Arg Lys Gly Phe Val Arg Leu Ala Leu Thr His Gly Ala Pro Leu Val			
	210	215	220	
	cca atc ttc tcc ttc ggg gag aat gac cta ttt gac cag att ccc aac			780
15	Pro Ile Phe Ser Phe Gly Glu Asn Asp Leu Phe Asp Gln Ile Pro Asn			
	225	230	235	
	tct tct ggc tcc tgg tta cgc tat atc cag aat cgg ttg cag aag atc			828
	Ser Ser Gly Ser Trp Leu Arg Tyr Ile Gln Asn Arg Leu Gln Lys Ile			
	240	245	250	
20	atg ggc atc tcc ctc cca ctc ttt cat ggc cgt ggt gtc ttc cag tac			876
	Met Gly Ile Ser Leu Pro Leu Phe His Gly Arg Gly Val Phe Gln Tyr			
	255	260	265	
	agc ttt ggt tta ata ccc tac cgc cgg ccc atc acc act gtg gtg ggg			924
	Ser Phe Gly Leu Ile Pro Tyr Arg Arg Pro Ile Thr Thr Val Val Gly			
25	270	275	280	285
	aag ccc atc gag gta cag aag acg ctg cat ccc tcg gag gag gag gtg			972
	Lys Pro Ile Glu Val Gln Lys Thr Leu His Pro Ser Glu Glu Glu Val			
	290	295	300	
	aac cag ctg cac cag cgt tat atc aaa gag ctg tgc aac ctc ttc gag			1020
30	Asn Gln Leu His Gln Arg Tyr Ile Lys Glu Leu Cys Asn Leu Phe Glu			
	305	310	315	
	gcc cac aaa ctt aag ttc aac atc cct gct gac cag cac ttg gag ttc			1068
	Ala His Lys Leu Lys Phe Asn Ile Pro Ala Asp Gln His Leu Glu Phe			
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	Ser Pro Gly Val Leu Val Arg Thr Gly His Thr Val Leu Thr Trp Gly	
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	atc acg ctg gtg ctc ttc ctg cac gat acc gag ctg cgg caa tgg gag	148
	Ile Thr Leu Val Leu Phe Leu His Asp Thr Glu Leu Arg Gln Trp Glu	
	25 30 35	
	gag cag ggg gag ctg ctc ctg ccc ctc acc ttc ctg ctc ctg gtg ctg	196
15	Glu Gln Gly Glu Leu Leu Leu Pro Leu Thr Phe Leu Leu Leu Val Leu	
	40 45 50 55	
	ggc tcc ctg ctg ctc tac ctc gct gtg tca ctc atg gac cct ggc tac	244
	Gly Ser Leu Leu Leu Tyr Leu Ala Val Ser Leu Met Asp Pro Gly Tyr	
	60 65 70	
20	gtg aat gtg cag ccc cag cct cag gag gag ctc aaa gag gag cag aca	292
	Val Asn Val Gln Pro Gln Pro Gln Glu Glu Leu Lys Glu Glu Gln Thr	
	75 80 85	
	gcc atg gtt cct cca gcc atc cct ctt cgg cgc tgc aga tac tgc ctg	340
	Ala Met Val Pro Pro Ala Ile Pro Leu Arg Arg Cys Arg Tyr Cys Leu	
25	90 95 100	
	gtg ctg cag ccc ctg agg gct cgg cac tgc cgt gag tgc cgc cgt tgc	388
	Val Leu Gln Pro Leu Arg Ala Arg His Cys Arg Glu Cys Arg Arg Cys	
	105 110 115	
	gtc cgc cgc tac gac cac cac tgc ccc tgg atg gag aac tgt gtg gga	436
30	Val Arg Arg Tyr Asp His His Cys Pro Trp Met Glu Asn Cys Val Gly	
	120 125 130 135	
	gag cgc aac cac cca ctc ttt gtg gtc tac ctg gcg ctg cag ctg gtg	484
	Glu Arg Asn His Pro Leu Phe Val Val Tyr Leu Ala Leu Gln Leu Val	
	140 145 150	
35	gtg ctt ctg tgg ggc ctg tac ctg gca tgg tca ggc ctc cgg ttc ttc	532

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Val Leu Leu Trp Gly Leu Tyr Leu Ala Trp Ser Gly Leu Arg Phe Phe
155 160 165
cag ccc tgg ggt ctg tgg ttg cgg tcc agc ggg ctc ctg ttc gcc acc 580
Gln Pro Trp Gly Leu Trp Leu Arg Ser Ser Gly Leu Leu Phe Ala Thr
5 170 175 180
ttc ctg ctg ctg tcc ctc ttc tgc ttg gtg gcc agc ctg ctc ctc gtc 628
Phe Leu Leu Leu Ser Leu Phe Ser Leu Val Ala Ser Leu Leu Leu Val
185 190 195
tcg cac ctc tac ctg gtg gcc agc aac acc acc acc tgg gaa ttc atc 676
10 Ser His Leu Tyr Leu Val Ala Ser Asn Thr Thr Thr Trp Glu Phe Ile
200 205 210 215
tcc tca cac cgc atc gcc tat ctc cgc cag cgc ccc agc aac ccc ttc 724
Ser Ser His Arg Ile Ala Tyr Leu Arg Gln Arg Pro Ser Asn Pro Phe
220 225 230
15 gac cga ggc ctg acc cgc aac ctg gcc cac ttc ttc tgt gga tgg ccc 772
Asp Arg Gly Leu Thr Arg Asn Leu Ala His Phe Phe Cys Gly Trp Pro
235 240 245
tca ggg tcc tgg gag acc ctc tgg gct gag gag gag gaa gag gcc agc 820
Ser Gly Ser Trp Glu Thr Leu Trp Ala Glu Glu Glu Glu Glu Gly Ser
20 250 255 260
agc cca gct gtt taggggtgct ggaggccggg ctaccgtett gtgectga 870
Ser Pro Ala Val
265
aaaccaagg ggcctgtcccc agctgggggtg agcgtcaga gggcctgggg ccctcaactcc 930
25 tgcccacgcc tcccagaccc cagaacggag cttcaagtca gacagatccc tgcccttggtg 990
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	Met Thr	
	1	
10	ctg ttt cac ttc ggg aac tgc ttc gct ctt gcc tac ttc ccc tac ttc	164
	Leu Phe His Phe Gly Asn Cys Phe Ala Leu Ala Tyr Phe Pro Tyr Phe	
	5 10 15	
	atc acc tac aag tgc agc ggc ctg tcc gag tac aac gcc ttc tgg aaa	212
	Ile Thr Tyr Lys Cys Ser Gly Leu Ser Glu Tyr Asn Ala Phe Trp Lys	
	20 25 30	
15	tgc gtc cag gct gga gtc acc tac ctc ttt gtc caa ctc tgc aag atg	260
	Cys Val Gln Ala Gly Val Thr Tyr Leu Phe Val Gln Leu Cys Lys Met	
	35 40 45 50	
	ctg ttc ttg gcc act ttc ttt ccc acc tgg gaa ggc ggc atc tat gac	308
	Leu Phe Leu Ala Thr Phe Phe Pro Thr Trp Glu Gly Gly Ile Tyr Asp	
20	55 60 65	
	ttc att ggg gag ttc atg aag gcc agc gtg gat gtg gca gac ctg ata	356
	Phe Ile Gly Glu Phe Met Lys Ala Ser Val Asp Val Ala Asp Leu Ile	
	70 75 80	
	ggc cta aac ctt gtc atg tcc cgg aat gcc ggc aag gga gag tac aag	404
25	Gly Leu Asn Leu Val Met Ser Arg Asn Ala Gly Lys Gly Glu Tyr Lys	
	85 90 95	
	atc atg gtt gct gcc ctg ggc tgg gcc act gct gag ctt att atg tcc	452
	Ile Met Val Ala Ala Leu Gly Trp Ala Thr Ala Glu Leu Ile Met Ser	
	100 105 110	
30	cgc tgc att ccc cta tgg gtc gga gcc cgg ggc att gag ttt gac tgg	500
	Arg Cys Ile Pro Leu Trp Val Gly Ala Arg Gly Ile Glu Phe Asp Trp	
	115 120 125 130	
	aag tac atc cag atg agc ata gac tcc aac atc agt ctg gtc cat tac	548
	Lys Tyr Ile Gln Met Ser Ile Asp Ser Asn Ile Ser Leu Val His Tyr	
35	135 140 145	

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atc gtc gcg tct gct cag gtc tgg atg ata aca cgc tat gat ctg tac 596
Ile Val Ala Ser Ala Gln Val Trp Met Ile Thr Arg Tyr Asp Leu Tyr
150 155 160

5 cac acc ttc cgg cca gct gtc ctc ctg ctg atg ttc ctc agt gtc tac 644
His Thr Phe Arg Pro Ala Val Leu Leu Leu Met Phe Leu Ser Val Tyr
165 170 175

aag gcc ttt gtt atg gag acc ttc gtc cac ctc tgc tcg ctg ggc agt 692
Lys Ala Phe Val Met Glu Thr Phe Val His Leu Cys Ser Leu Gly Ser
180 185 190

10 tgg gca gct cta ctg gcc cga gca gtg gta acg ggg ctg ctg gcc ctc 740
Trp Ala Ala Leu Leu Ala Arg Ala Val Val Thr Gly Leu Leu Ala Leu
195 200 205 210

age act ttg gcc ctg tat gtc gcc gtt gtc aat gtg cac tcc taggcttg 790
Ser Thr Leu Ala Leu Tyr Val Ala Val Val Asn Val His Ser
15 215 220

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gtatttggaag agtt 864

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Met Ala Val Leu Ala Pro Leu Ile Ala
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ctc gtg tat tcg gtg ccg cga ott tca cga tgg ctc gcc caa cct tac 99
Leu Val Tyr Ser Val Pro Arg Leu Ser Arg Trp Leu Ala Gln Pro Tyr
10 15 20 25

tac ctt ctg tcg gcc ctg ctc tct gct gcc ttc cta ctc gtg agg aaa 147
35 Tyr Leu Leu Ser Ala Leu Leu Ser Ala Ala Phe Leu Leu Val Arg Lys

		30	35	40	
	ctg ccg ccg ctc tgc cac ggt ctg ccc acc caa cgc gaa gac ggt aac				195
	Leu Pro Pro Leu Cys His Gly Leu Pro Thr Gln Arg Glu Asp Gly Asn				
	45	50	55		
5	ccg tgt gac ttt gac tgg aga gaa gtg gag atc ctg atg ttt ctc agt				243
	Pro Cys Asp Phe Asp Trp Arg Glu Val Glu Ile Leu Met Phe Leu Ser				
	60	65	70		
	gcc att gtg atg atg aag aac cgc aga tcc atg ttc ctg atg acg tgc				291
	Ala Ile Val Met Met Lys Asn Arg Arg Ser Met Phe Leu Met Thr Cys				
10	75	80	85		
	aaa ccc ccc cta tat atg ggc cct gag tat atc aag tac ttc aat gat				339
	Lys Pro Pro Leu Tyr Met Gly Pro Glu Tyr Ile Lys Tyr Phe Asn Asp				
	90	95	100	105	
	aaa acc att gat gag gaa cta gaa cgg gac aag agg gtc act tgg att				387
15	Lys Thr Ile Asp Glu Glu Leu Glu Arg Asp Lys Arg Val Thr Trp Ile				
	110	115	120		
	gtg gag ttc ttt gcc aat tgg tct aat gac tgc caa tca ttt gcc cct				435
	Val Glu Phe Phe Ala Asn Trp Ser Asn Asp Cys Gln Ser Phe Ala Pro				
	125	130	135		
20	atc tat gct gac ctc tcc ctt aaa tac aac tgt aca ggg cta aat ttt				483
	Ile Tyr Ala Asp Leu Ser Leu Lys Tyr Asn Cys Thr Gly Leu Asn Phe				
	140	145	150		
	ggg aag gtg gat gtt gga cgc tat act gat gtt agt acg cgg tac aaa				531
	Gly Lys Val Asp Val Gly Arg Tyr Thr Asp Val Ser Thr Arg Tyr Lys				
25	155	160	165		
	gtg agc aca tca ccc ctc acc aag caa ctc cct acc ctg atc ctg ttc				579
	Val Ser Thr Ser Pro Leu Thr Lys Gln Leu Pro Thr Leu Ile Leu Phe				
	170	175	180	185	
	caa ggt ggc aag gag gca atg cgg cgg cca cag att gac aag aaa gga				627
30	Gln Gly Gly Lys Glu Ala Met Arg Arg Pro Gln Ile Asp Lys Lys Gly				
	190	195	200		
	cgg gct gtc tca tgg acc ttc tct gag gag aat gtg atc cga gaa ttt				675
	Arg Ala Val Ser Trp Thr Phe Ser Glu Glu Asn Val Ile Arg Glu Phe				
	205	210	215		
35	aac tta aat gag cta tac cag cgg gcc aag aaa cta tca aag gct gga				723

	ccg ttc atc agc gag gcg gcc gtg cgg ggc aac gcc gcc gtc ctg gat	218
	Pro Phe Ile Ser Glu Ala Ala Val Arg Gly Asn Ala Ala Val Leu Asp	
	15 20 25	
	tat tgc cgg acc tcg gtg tca gcg ctg tcg ggg gcc acg gcc ggc atc	266
5	Tyr Cys Arg Thr Ser Val Ser Ala Leu Ser Gly Ala Thr Ala Gly Ile	
	30 35 40	
	ctc ggc ctc acc ggc ctc tac ggc ttc atc ttc tac ctg ctc gcc tcc	314
	Leu Gly Leu Thr Gly Leu Tyr Gly Phe Ile Phe Tyr Leu Leu Ala Ser	
	45 50 55	
10	gtc ctg ctc tcc ctg ctc ctc att ctc aag gcg gga agg agg tgg aac	362
	Val Leu Leu Ser Leu Leu Leu Ile Leu Lys Ala Gly Arg Arg Trp Asn	
	60 65 70 75	
	aaa tat ttc aaa tca cgg aga cct ctc ttt aca gga ggc ctc atc ggg	410
	Lys Tyr Phe Lys Ser Arg Arg Pro Leu Phe Thr Gly Gly Leu Ile Gly	
15	80 85 90	
	ggc ctc ttc acc tac gtc ctg ttc tgg acg ttc ctc tac ggc atg gtg	458
	Gly Leu Phe Thr Tyr Val Leu Phe Trp Thr Phe Leu Tyr Gly Met Val	
	95 100 105	
	cac gtc tac tgaaatgggg gcccggggga cttttttaaa aaa	500
20	His Val Tyr	
	110	
	ccagatcggg aggactgtgg ccagcaatta acaccatgta gacttcctta gttottaagt	560
	ggttgaattc gctgcttggt ctgtaacggt ataaataatt tatactctgaa gacggagagc	620
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	Met Val Tyr Ile Ser Asn Gly Gln Val Leu Asp Ser Arg Ser	
	1 5 10	
5	cag tct cca tgg aga tta tct ttg ata aca gat ttc ttc tgg gga ata	157
	Gln Ser Pro Trp Arg Leu Ser Leu Ile Thr Asp Phe Phe Trp Gly Ile	
	15 20 25 30	
	gct gag ttt gtg gtt ttg ttt ttc aaa act ctg ctt cag caa gat gtg	205
	Ala Glu Phe Val Val Leu Phe Phe Lys Thr Leu Leu Gln Gln Asp Val	
	35 40 45	
10	aaa aaa aga aga agc tat gga aac tca tct gat tcc aga tat gat gat	253
	Lys Lys Arg Arg Ser Tyr Gly Asn Ser Ser Asp Ser Arg Tyr Asp Asp	
	50 55 60	
	gga aga ggg cca cca gga aac cct ccc cga aga atg ggt aga atc aat	301
	Gly Arg Gly Pro Pro Gly Asn Pro Pro Arg Arg Met Gly Arg Ile Asn	
15	65 70 75	
	cat ctg cgt ggc cct agt ccc cct cca atg gct ggt gga tgaggaaggt	350
	His Leu Arg Gly Pro Ser Pro Pro Pro Met Ala Gly Gly	
	80 85 90	
20	aaatgtctgc tctaagaagc agacaaccgg acatgcgcat tcatagcaga aggaaaccat	410
	caagaagtgg aaggctgacc atgatgagca gtagatgaat gtgtatgtct aaacaaggac	470
	tgtctgtgt cctcacagat gaatgaggtc atgctgggaa ttccctctgc agggaaactgg	530
	cctgactgac atgcagttcc ataaatgcag atgtttgtct cattaccttt ttgtatagtt	590
	tattaaagta ttaatatagt ttaataagt aaatatTTTT aggttgacaga atggactcct	650
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5	aag agc ctt ctg ctg gtc ccc agt gcc ctc tcc ctc ctg ctc gcc ctc	151
	Lys Ser Leu Leu Leu Val Pro Ser Ala Leu Ser Leu Leu Leu Ala Leu	
	20 25 30	
	ctc ctg cct cac tgc cag aag ctc ttt gtg tat gac ctt cac gca gtc	199
	Leu Leu Pro His Cys Gln Lys Leu Phe Val Tyr Asp Leu His Ala Val	
	35 40 45	
10	aag aac gac ttc cag att tgg agg ttg ata tgt gga aga ata att tgc	247
	Lys Asn Asp Phe Gln Ile Trp Arg Leu Ile Cys Gly Arg Ile Ile Cys	
	50 55 60	
	ctt gat ttg aaa gat act ttc tgc agt agt ctg ctt att tat aat ttt	295
	Leu Asp Leu Lys Asp Thr Phe Cys Ser Ser Leu Leu Ile Tyr Asn Phe	
15	65 70 75 80	
	agg ata ttt gaa aga aga tat gga agc aga aaa ttt gca tcc ttt ttg	343
	Arg Ile Phe Glu Arg Arg Tyr Gly Ser Arg Lys Phe Ala Ser Phe Leu	
	85 90 95	
	ctg ggt tcc tgg gtt ttg tca gcc tta ttt gac ttt ctc ctc att gaa	391
20	Leu Gly Ser Trp Val Leu Ser Ala Leu Phe Asp Phe Leu Leu Ile Glu	
	100 105 110	
	gct atg cag tat ttc ttt ggc atc act gca gct agt aat ttg cct tct	439
	Ala Met Gln Tyr Phe Phe Gly Ile Thr Ala Ala Ser Asn Leu Pro Ser	
	115 120 125	
25	gga ttc ctg gca cct gtg ttt gct ctg ttt gta cca ttt tac tgc tcc	487
	Gly Phe Leu Ala Pro Val Phe Ala Leu Phe Val Pro Phe Tyr Cys Ser	
	130 135 140	
	ata cca aga gtc caa gtg gca caa att ctg ggt ccg ttg tcc atc aca	535
	Ile Pro Arg Val Gln Val Ala Gln Ile Leu Gly Pro Leu Ser Ile Thr	
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	aac aag aca ttg att tat ata ttg gga ctg cag ctt ttc acc tct ggt	583
	Asn Lys Thr Leu Ile Tyr Ile Leu Gly Leu Gln Leu Phe Thr Ser Gly	
	165 170 175	
	tcc tac atc tgg att gta gcc ata agt gga ctt atg tcc ggt ctg tgc	631
35	Ser Tyr Ile Trp Ile Val Ala Ile Ser Gly Leu Met Ser Gly Leu Cys	

	180	185	190	
	tac gac agc aaa atg ttc cag gtg cat cag gtg ctc tgc atc ccc agc			679
	Tyr Asp Ser Lys Met Phe Gln Val His Gln Val Leu Cys Ile Pro Ser			
	195	200	205	
5	tgg atg gca aaa ttc ttt tct tgg aca ctt gaa ccc atc ttc tct tct			727
	Trp Met Ala Lys Phe Phe Ser Trp Thr Leu Glu Pro Ile Phe Ser Ser			
	210	215	220	
	tca gaa ccc acc agc gaa gcc aga att ggg atg gga gcc acg ctg gac			775
	Ser Glu Pro Thr Ser Glu Ala Arg Ile Gly Met Gly Ala Thr Leu Asp			
10	225	230	235	240
	atc cag aga cag cag aga atg gag ctg ctg gac cgg cag ctg atg ttc			823
	Ile Gln Arg Gln Gln Arg Met Glu Leu Leu Asp Arg Gln Leu Met Phe			
	245	250	255	
	tct cag ttt gca caa ggg agg cga cag aga cag cag cag gga gga atg			871
15	Ser Gln Phe Ala Gln Gly Arg Arg Gln Arg Gln Gln Gln Gly Gly Met			
	260	265	270	
	atc aat tgg aat cgt ctt ttt cct cct tta cgt cag cga caa aac gta			919
	Ile Asn Trp Asn Arg Leu Phe Pro Pro Leu Arg Gln Arg Gln Asn Val			
	275	280	285	
20	aac tat cag ggc ggt cgg cag tct gag cca gca gcg ccc cct cta gaa			967
	Asn Tyr Gln Gly Gly Arg Gln Ser Glu Pro Ala Ala Pro Pro Leu Glu			
	290	295	300	
	gtt tct gag gaa cag gtc gcc cgg ctc atg gag atg gga ttt tcc aga			1015
	Val Ser Glu Glu Gln Val Ala Arg Leu Met Glu Met Gly Phe Ser Arg			
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	ggg gat gct ttg gaa gcc ctg aga gct tca aac aat gac ctc aat gtc			1063
	Gly Asp Ala Leu Glu Ala Leu Arg Ala Ser Asn Asn Asp Leu Asn Val			
	325	330	335	
	gcc acc aac ttc ctg ctg cag cac tgatagtcac aggccaacac tgg			1110
30	Ala Thr Asn Phe Leu Leu Gln His			
	340			
	gaccggaccg gcagccgagt gacagtgcgt ggtccccacc atcagatcag cccggggacc			1170
	gagcatctct ggtgctgatg ttcttgtggg aagagggagg ttccaccgca ccctgcct			1230
	caaccgcaag actggtgccg ttttagtggt gagataagtt tgccattaca ttagcatgta			1290
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<221> CDS

<222> (211)...(1497)

<400> 150

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 cctggcgcgc acctgctcaa gaccagggtc ctgccaaagc ctaggagggc gcgtgccagg 180
 ggcgctaggg aactgaggag cgcgcgcgcc atg ggg ccg ccg cct ggg gcc 231

Met Gly Pro Pro Pro Gly Ala

30

1

5

ggg gtc tcc tgc cgc ggt ggc tgc ggc ttt tcc aga ttg ctg gca tgg 279
 Gly Val Ser Cys Arg Gly Gly Cys Gly Phe Ser Arg Leu Leu Ala Trp

10

15

20

tgc ttc ctg ctg gcc ctg agt ccg cag gca ccc ggt tcc cgg ggg gct 327
 35 Cys Phe Leu Leu Ala Leu Ser Pro Gln Ala Pro Gly Ser Arg Gly Ala

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	25	30	35	
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	Glu Ala Val Trp Thr Ala Tyr Leu Asn Val Ser Trp Arg Val Pro His			
	40	45	50	55
5	acg gga gtg aac cgt acg gtg tgg gag ctg agc gag gag ggc gtg tac			423
	Thr Gly Val Asn Arg Thr Val Trp Glu Leu Ser Glu Glu Gly Val Tyr			
	60	65	70	
	ggc cag gac tcg ccg ctg gag cct gtg gct ggg gtc ctg gta ccg ccc			471
	Gly Gln Asp Ser Pro Leu Glu Pro Val Ala Gly Val Leu Val Pro Pro			
10	75	80	85	
	gac ggg ccc ggg gcg ctt aac gcc tgt aac ccg cac acg aat ttc acg			519
	Asp Gly Pro Gly Ala Leu Asn Ala Cys Asn Pro His Thr Asn Phe Thr			
	90	95	100	
	gtg ccc acg gtt tgg gga agc acc gtg caa gtc tct tgg ttg gcc ctc			567
15	Val Pro Thr Val Trp Gly Ser Thr Val Gln Val Ser Trp Leu Ala Leu			
	105	110	115	
	atc caa cgc ggc ggg ggc tgc acc ttc gca gac aag atc cat ctg gct			615
	Ile Gln Arg Gly Gly Gly Cys Thr Phe Ala Asp Lys Ile His Leu Ala			
	120	125	130	135
20	tat gag aga ggg gcg tct gga gcc gtc atc ttt aac ttc ccc ggg acc			663
	Tyr Glu Arg Gly Ala Ser Gly Ala Val Ile Phe Asn Phe Pro Gly Thr			
	140	145	150	
	cgc aat gag gtc atc ccc atg tct cac ccg ggt gca gta gac att gtt			711
	Arg Asn Glu Val Ile Pro Met Ser His Pro Gly Ala Val Asp Ile Val			
25	155	160	165	
	gca atc atg atc ggc aat ctg aaa ggc aca aaa att ctg caa tct att			759
	Ala Ile Met Ile Gly Asn Leu Lys Gly Thr Lys Ile Leu Gln Ser Ile			
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	caa aga ggc ata caa gtg aca atg gtc ata gaa gta ggg aaa aaa cat			807
30	Gln Arg Gly Ile Gln Val Thr Met Val Ile Glu Val Gly Lys Lys His			
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	ggc cct tgg gtg aat cac tat tca att ttt ttc gtt tct gtg tcc ttt			855
	Gly Pro Trp Val Asn His Tyr Ser Ile Phe Phe Val Ser Val Ser Phe			
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	Arg Arg Leu Arg Asn Ala Arg Ala Gln Ser Arg Lys Gln Arg Gln Leu	
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	aag gca gat gct aaa aaa gct att gga agg ctt caa cta cgc aca ctg	999
	Lys Ala Asp Ala Lys Lys Ala Ile Gly Arg Leu Gln Leu Arg Thr Leu	
	250 255 260	
	aaa caa gga gac aag gaa att ggc cct gat gga gat agt tgt gct gtg	1047
10	Lys Gln Gly Asp Lys Glu Ile Gly Pro Asp Gly Asp Ser Cys Ala Val	
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	tgc att gaa ttg tat aaa cca aat gat ttg gta cgc atc tta acg tgc	1095
	Cys Ile Glu Leu Tyr Lys Pro Asn Asp Leu Val Arg Ile Leu Thr Cys	
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	Asn His Ile Phe His Lys Thr Cys Val Asp Pro Trp Leu Leu Glu His	
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	Arg Thr Cys Pro Met Cys Lys Cys Asp Ile Leu Lys Ala Leu Gly Ile	
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	Glu Val Asp Val Glu Asp Gly Ser Val Ser Leu Gln Val Pro Val Ser	
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25	Asn Glu Ile Ser Asn Ser Ala Ser Ser His Glu Glu Asp Asn Arg Ser	
	345 350 355	
	gag acc gca tca tct gga tat gct tca gta cag gga aca gat gaa ccg	1335
	Glu Thr Ala Ser Ser Gly Tyr Ala Ser Val Gln Gly Thr Asp Glu Pro	
	360 365 370 375	
30	cct ctg gag gaa cac gtg cag tca aca aat gaa agt cta cag ctg gta	1383
	Pro Leu Glu Glu His Val Gln Ser Thr Asn Glu Ser Leu Gln Leu Val	
	380 385 390	
	aac cat gaa gca aat tct gtg gca gtg gat gtt att cct cat gtt gac	1431
	Asn His Glu Ala Asn Ser Val Ala Val Asp Val Ile Pro His Val Asp	
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